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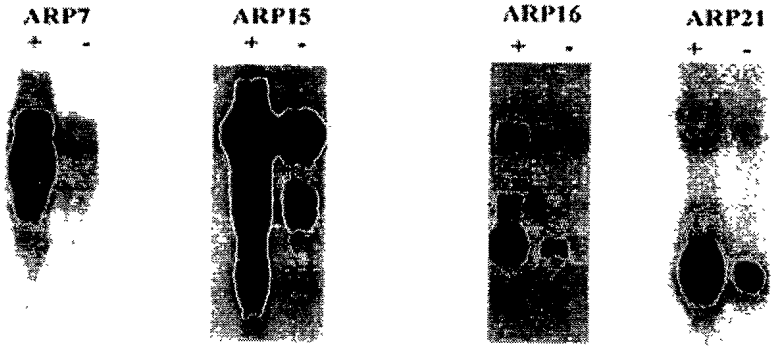
(54) Title: ANDROGEN REGULATED NUCLEIC ACID MOLECULES AND ENCODED PROTEINS



(57) Abstract: The present invention provides novel androgen regulated nucleic acid molecules. Related polypeptides and diagnostic methods also are provided.

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ANDROGEN REGULATED NUCLEIC ACID MOLECULES AND ENCODED PROTEINS

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

This invention relates generally to cancer and, more specifically, to prostate-specific genes that can be used to diagnose and treat prostate cancer.

BACKGROUND INFORMATION

Cancer is currently the second leading cause of mortality in the United States. However, it is estimated that by the year 2000 cancer will surpass heart disease and become the leading cause of death in the United States. Prostate cancer is the most common non-cutaneous cancer in the United States and the second leading cause of male cancer mortality.

Cancerous tumors result when a cell escapes from its normal growth regulatory mechanisms and proliferates in an uncontrolled fashion. As a result of such uncontrolled proliferation, cancerous tumors usually invade neighboring tissues and spread by lymph or blood stream to create secondary or metastatic growths in other tissues. If untreated, cancerous tumors follow a fatal course. Prostate cancer, due to its slow growth profile, is an excellent candidate for early detection and therapeutic intervention.

During the last decade, most advances in prostate cancer research have focused on prostate specific antigen (PSA), a member of the serine protease

family that exhibits a prostate-specific expression profile. Serum PSA remains the most widely used tumor marker for monitoring prostate cancer, but its specificity is limited by a high frequency of falsely elevated values in men with benign prostatic hyperplasia (BPH). Other biomarkers of prostate cancer progression have proven to be of limited clinical use in recent surveys because they are not uniformly elevated in men with advanced prostate cancer. Due to the limitations of currently available biomarkers, the identification and characterization of prostate specific genes is essential to the development of more accurate diagnostic methods and therapeutic targets. In many cases, the clinical potential of novel tumor markers can be optimized by utilizing them in combination with other tumor markers in the development of diagnostic and treatment modalities.

Normal prostate tissue consists of three distinct non-stromal cell populations, luminal secretory cells, basal cells, and endocrine paracrine cells. Phenotypic similarities between normal luminal cells and prostate cancer cells, including the expression of PSA, have suggested that prostate adenocarcinomas derive from luminal cells. However, a number of recent studies suggest that at least some prostate cancers can arise from the transformation of basal cells and report the expression of various genes in normal prostate basal cells as well as in prostate carcinoma cells. These genes include prostate stem cell antigen (PSCA), c-met and Bcl-2. Because none of these genes is universally expressed in all basal cells and prostate carcinomas, the utility of these genes as diagnostic markers is limited. Likewise, because PSA is expressed in luminal secretory cells in normal prostate tissue, this antigen has limited utility as a marker for basal cell derived carcinomas.

Thus, there exists a need for the identification of additional prostate specific genes that can be used as diagnostic markers and therapeutic targets for prostate cancer. The present invention satisfies this need and provides related advantages as well.

SUMMARY OF THE INVENTION

The present invention provides androgen responsive prostate specific (ARP) nucleic acid and polypeptide molecules.

The present invention provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP15 binding agent that selectively binds an ARP15 polypeptide; determining a test expression level of ARP15 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP15 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in such a method can include, for example, prostate tissue, or can be, for example, blood, serum, urine or semen. In one embodiment, the ARP15 binding agent that selectively binds the ARP15 polypeptide is an antibody.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP15 nucleic acid molecule; determining a test expression level of ARP15 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of

ARP15 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A sample useful in such a method of the invention can include, for example, prostate tissue, or can be, for example, blood, urine or semen. An ARP15 nucleic acid molecule useful in the invention can include, for example, at least 10 contiguous nucleotides of SEQ ID NO: 3. An ARP15 nucleic acid molecule useful in a method of the invention further can have a length of, for example, 15 to 35 nucleotides.

Further provided herein is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP15 regulatory agent.

The present invention provides a substantially pure ARP7 nucleic acid molecule which includes the nucleotide sequence shown as SEQ ID NO: 1. The invention also provides a substantially pure ARP7 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-445 of SEQ ID NO: 1.

Further provided by the invention is method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method is practiced by contacting a sample from the individual with an ARP7 nucleic acid molecule; determining a test expression level of ARP7 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP7 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a prostate

tissue sample. In another embodiment, the method is practiced with a sample of blood, urine or semen. In a further embodiment, the method is practiced with an ARP7 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 1. In yet a further embodiment, the method is practiced with an ARP7 nucleic acid molecule that has a length of 15 to 35 nucleotides.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method includes the steps of contacting a specimen from the individual with an ARP7 binding agent that selectively binds an ARP7 polypeptide; determining a test expression level of ARP7 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP7 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced with a specimen that includes, for example, prostate tissue, or with a specimen which is blood, serum, urine or semen. If desired, a method of the invention for diagnosing or predicting susceptibility to a prostate neoplastic condition can be practiced with an ARP7 binding agent which is an antibody.

Also provided by the invention is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP7 regulatory agent.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP16 nucleic acid

molecule; determining a test expression level of ARP16 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP16 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in the methods of the invention include, for example, prostate tissue samples as well as samples of blood, urine or semen. In one embodiment, a method of the invention is practiced with an ARP16 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 5. In another embodiment, a method of the invention is practiced with an ARP16 nucleic acid molecule which has a length of 15 to 35 nucleotides.

Also provided by the invention is a substantially pure ARP16 polypeptide fragment which has at least eight contiguous amino acids of residues 26-100 of SEQ ID NO: 6. Also provided herein is an ARP16 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of residues 26-100 of SEQ ID NO: 6. Such an ARP16 binding agent can be, for example, an antibody.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP16 binding agent that selectively binds an ARP16 polypeptide; determining a test expression level of ARP16 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP16 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the

individual. A specimen useful for diagnosing or predicting susceptibility to a prostate neoplastic condition can include, for example, prostate tissue, or can be, for example, a specimen of blood, serum, urine or semen. In one embodiment, the ARP16 binding agent that selectively binds the ARP16 polypeptide is an antibody.

Further provided herein is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP16 regulatory agent.

The invention additionally provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method includes the steps of contacting a sample from the individual with an ARP8 nucleic acid molecule; determining a test expression level of ARP8 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP8 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the sample includes prostate tissue. In other embodiments, the sample is blood, urine or semen. In another embodiment, the ARP8 nucleic acid molecule contains at least 10 contiguous nucleotides of SEQ ID NO:7. In a further embodiment, the ARP8 nucleic acid molecule has a length of 15 to 35 nucleotides.

The present invention further provides a substantially pure ARP8 polypeptide that contains an amino acid sequence having at least 65% amino acid identity with SEQ ID NO: 8. Such an ARP8 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 8. In addition, there is provided herein a

substantially pure ARP8 polypeptide fragment, which includes at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8. In one embodiment, the ARP8 fragment has at least eight contiguous amino acids of residues 249-576 of SEQ ID NO: 8.

Also provided herein is an ARP8 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8, for example, an antibody that selectively binds at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8. In addition, the invention provides an ARP8 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of residues 249-576 of SEQ ID NO: 8. Such an ARP8 binding agent can be, for example, an antibody.

There is further provided herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP8 binding agent that selectively binds an ARP8 polypeptide; determining a test expression level of ARP8 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP8 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a specimen that includes prostate tissue, or with a specimen which is blood, serum, urine or semen. In one embodiment, the ARP8 binding agent that selectively binds the ARP8 polypeptide is an antibody.

Also provided herein is a method for treating or reducing the severity of a prostate neoplastic

condition in an individual by administering to the individual an ARP8 regulatory agent.

Further provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method is practiced by contacting a sample from the individual with an ARP9 nucleic acid molecule; determining a test expression level of ARP9 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP9 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a sample that includes prostate tissue. In other embodiments, a method of the invention is practiced with a sample of blood, urine or semen. In a further embodiment, a method of the invention is practiced with an ARP9 nucleic acid molecule that includes at least 10 contiguous nucleotides of SEQ ID NO: 9. In yet a further embodiment, a method of the invention is practiced with an ARP9 nucleic acid molecule having a length of 15 to 35 nucleotides.

The invention also provides a substantially pure ARP9 polypeptide that includes an amino acid sequence having at least 65% amino acid identity with SEQ ID NO: 10. Such an ARP9 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 10. Substantially pure ARP9 polypeptide fragments also are provided herein. The ARP9 fragments of the invention have at least eight contiguous amino acids of residues 1-83 of SEQ ID NO: 10. In one embodiment, such

an ARP9 fragment of the invention has at least eight contiguous amino acids of residues 47-62 of SEQ ID NO: 10.

The invention also provides an ARP9 binding agent that includes a molecule that selectively binds at least eight contiguous amino acids of residues 1-83 of SEQ ID NO: 10. In one embodiment, the ARP9 binding agent includes a molecule that selectively binds at least eight contiguous amino acids of residues 47-62 of SEQ ID NO: 10. An ARP9 binding agent of the invention can be, for example, an antibody.

The present invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, in which a specimen from the individual is contacted with an ARP9 binding agent that selectively binds an ARP9 polypeptide; a test expression level of ARP9 polypeptide in the specimen is determined; and the test expression level is compared to a non-neoplastic control expression level of ARP9 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced with a specimen containing, for example, prostate tissue, or, for example, with a blood, serum, urine or semen specimen. If desired, a method of the invention can be practiced with an ARP9 binding agent which is an antibody.

Further provided herein is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP9 regulatory agent.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method includes the steps of contacting a sample from the individual with an ARP13 nucleic acid molecule; determining a test expression level of ARP13 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP13 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a sample which includes prostate tissue or, for example, with a blood, urine or semen sample. A variety of ARP13 nucleic acid molecules are useful in the methods of the invention including, for example, ARP13 nucleic acid molecules which include at least 10 contiguous nucleotides of SEQ ID NO: 11 and ARP13 nucleic acid molecules of 15 to 35 nucleotides in length.

Also provided herein is a substantially pure ARP13 polypeptide, which has an amino acid sequence having at least 90% amino acid identity with SEQ ID NO: 12. As an example, a substantially pure ARP13 polypeptide of the invention can have the amino acid sequence shown as SEQ ID NO: 12. The invention additionally provides a substantially pure ARP13 polypeptide fragment that includes at least eight contiguous amino acids of SEQ ID NO: 12.

There further is provided herein an ARP13 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 12. In one embodiment, the ARP13 binding agent is an antibody.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP13 binding agent that selectively binds an ARP13 polypeptide; determining a test expression level of ARP13 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP13 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A variety of specimens are useful in a method of the invention for diagnosing or predicting susceptibility to a prostate neoplastic condition, including, but not limited to, prostate tissue, blood, serum, urine and semen. An ARP13 binding agent useful in a method of the invention can be, for example, an antibody.

Further provided herein is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP13 regulatory agent.

There further is provided herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP20 nucleic acid molecule; determining a test expression level of ARP20 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP20 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in a method of the invention include prostate tissue, blood, urine and semen. In one

embodiment, a method of the invention is practiced with an ARP20 nucleic acid molecule which includes at least 10 contiguous nucleotides of SEQ ID NO: 13. In another embodiment, a method of the invention is practiced with an ARP20 nucleic acid molecule having a length of 15 to 35 nucleotides.

Further provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method is practiced by contacting a specimen from the individual with an ARP20 binding agent that selectively binds an ARP20 polypeptide; determining a test expression level of ARP20 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP20 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a specimen of prostate tissue. In another embodiment, a method of the invention is practiced with a blood, serum, urine or semen specimen. In a further embodiment, a method of the invention is practiced with an ARP20 binding agent which is an antibody.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP20 regulatory agent.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method includes the steps of contacting a sample from the individual with an ARP24 nucleic acid molecule; determining a test

expression level of ARP24 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP24 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a sample containing prostate tissue. In other embodiments, a method of the invention is practiced with a sample of blood, urine or semen. In yet further embodiments, a method of the invention is practiced with an ARP24 nucleic acid molecule that contains at least 10 contiguous nucleotides of SEQ ID NO: 15 or is 15 to 35 nucleotides in length.

Further provided herein is a substantially pure ARP24 polypeptide that includes an amino acid sequence having at least 30% amino acid identity with SEQ ID NO: 16. A substantially pure ARP24 polypeptide of the invention can have, for example, the amino acid sequence shown as SEQ ID NO: 16. The invention also provides a substantially pure ARP24 polypeptide fragment which contains at least eight contiguous amino acids of SEQ ID NO: 16.

In addition, there is provided herein an ARP24 binding agent that includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 16. In one embodiment, the ARP24 binding agent is an antibody.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP24 binding agent that selectively binds an ARP24 polypeptide; determining

a test expression level of ARP24 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP24 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in a method of the invention include prostate tissue, blood, urine and semen. In one embodiment, a method of the invention is practiced with an ARP24 nucleic acid molecule having a length of 15 to 35 nucleotides.

Further provided herein is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP24 regulatory agent.

The present invention further provides a substantially pure ARP26 nucleic acid which includes the nucleotide sequence shown as SEQ ID NO: 17. The invention also provides a substantially pure ARP26 nucleic acid molecule of the invention that includes at least 10 contiguous nucleotides of nucleotides 1404-1516 of SEQ ID NO: 17.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. A method of the invention includes the steps of contacting a sample from the individual with an ARP26 nucleic acid molecule; determining a test expression level of ARP26 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP26 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples

useful in a method of the invention include prostate tissue, blood, urine and semen. In one embodiment, a method of the invention is practiced with an ARP26 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 17. In another embodiment, a method of the invention is practiced with an ARP26 nucleic acid molecule having a length of 15 to 35 nucleotides.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP26 binding agent that selectively binds an ARP26 polypeptide; determining a test expression level of ARP26 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP26 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. In one embodiment, the ARP26 binding agent is an antibody.

The invention also provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP26 regulatory agent.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, in which a sample from the individual is contacted with an ARP28 nucleic acid molecule; a test expression level of ARP28 RNA in the sample is determined; and the test expression level

is compared to a non-neoplastic control expression level of ARP28 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the sample contacted with an ARP28 nucleic acid molecule contains prostate tissue. In other embodiments, the sample is blood, urine or semen sample. In another embodiment, the ARP28 nucleic acid molecule contains at least 10 contiguous nucleotides of SEQ ID NO: 19. In a further embodiment, the ARP28 nucleic acid molecule has a length of 15 to 35 nucleotides.

The invention further provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP28 binding agent the selectively binds an ARP28 polypeptide; determining a test expression level of ARP28 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP28 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. ARP28 binding agents useful in the methods of the invention include, but are not limited to, antibodies.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP28 regulatory agent.

The present invention also provides a substantially pure ARP30 nucleic acid molecule that includes at least 10 contiguous nucleotides of nucleotides 2346-2796 of SEQ ID NO: 21.

The invention also provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. This method includes the steps of contacting a sample from the individual with an ARP30 nucleic acid molecule containing at least 10 contiguous nucleotides of nucleotides 1-1829 or nucleotides 2346-3318 of SEQ ID NO: 21; determining a test expression level of ARP30 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP30 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a sample containing prostate tissue. In other embodiments, a method of the invention is practiced with a blood, urine or semen sample. In a further embodiment, a method of the invention is practiced with an ARP30 nucleic acid molecule having at least 10 contiguous nucleotides of nucleotides 2346-3318 of SEQ ID NO: 21. In yet a further embodiment, a method of the invention is practiced with an ARP30 nucleic acid molecule having a length of 15 to 35 nucleotides.

The invention also provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP30 binding agent that selectively binds an ARP30 polypeptide; determining a test expression level of ARP30 polypeptide in the specimen; and comparing the test expression level to a

non-neoplastic control expression level of ARP30 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. ARP30 binding agents useful in the methods of the invention include, but are not limited to, antibodies.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP30 regulatory agent.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP33 nucleic acid molecule; determining a test expression level of ARP33 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP33 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in the invention can include, for example, prostate tissue. Samples useful in the invention also can be samples of blood, urine or semen. A variety of ARP33 nucleic acid molecules are useful in the methods of the invention including, for example, ARP33 nucleic acid molecules that include at least 10 contiguous nucleotides of SEQ ID NO: 23 or ARP33 nucleotide acid molecules of 15 to 35 nucleotides in length.

The invention also provides a substantially pure ARP33 polypeptide that includes an amino acid sequence having at least 70% amino acid identity with SEQ ID NO: 24. Such a substantially pure ARP33 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 24. Also provided herein is a substantially pure ARP33 polypeptide fragment that includes at least eight contiguous amino acids of residues 1-132 or 251-405 of SEQ ID NO: 24.

The present invention also provides an ARP33 binding agent that includes a molecule that selectively binds at least eight contiguous amino acids of residues 1-132 or 251-405 of SEQ ID NO: 24. Such an ARP33 binding agent can be, for example, an antibody.

The invention also provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP33 binding agent that selectively binds an ARP33 polypeptide; determining a test expression level of ARP33 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP33 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. ARP33 binding agents useful in the methods of the invention encompass, without limitation, antibodies.

The invention further provides herein a method for treating or reducing the severity of a prostate

neoplastic condition in an individual by administering to the individual an ARP33 regulatory agent.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP11 binding agent that selectively binds an ARP11 polypeptide; determining a test expression level of ARP11 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP11 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. The method can be practiced with, for example, a prostate tissue specimen, or with a specimen of blood, serum, urine or semen. In one embodiment, a method of the invention is practiced with an ARP11 binding agent which is an antibody.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP11 regulatory agent.

The invention also provides a substantially pure ARP6 nucleic acid molecule that includes the nucleotide sequence shown as SEQ ID NO: 25. Further provided herein is a substantially pure ARP6 nucleic acid molecule that contains at least 10 contiguous nucleotides of nucleotides 505-526 of SEQ ID NO: 25.

The invention additionally provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP6 nucleic acid

molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 25; determining a test expression level of ARP6 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP6 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a prostate tissue sample. In another embodiment, the method is practiced with a sample of blood, urine or semen. In a further embodiment, the method is practiced with an ARP6 nucleic acid molecule having a length of 15 to 35 nucleotides.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP6 regulatory agent.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP10 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 26; determining a test expression level of ARP10 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP10 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a blood, urine or semen sample. In a further embodiment, the method is practiced with an ARP10 nucleic acid molecule of 15 to 35 nucleotides in length.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP10 regulatory agent.

The present invention further provides a substantially pure ARP12 nucleic acid molecule that contains the nucleotide sequence shown as SEQ ID NO: 27. In addition, the invention provides a substantially pure ARP12 nucleic acid molecule that contains at least 10 contiguous nucleotides of nucleotides 1635-1659 of SEQ ID NO: 27.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. This method includes the steps of contacting a sample from the individual with an ARP12 nucleic acid molecule containing at least 10 contiguous nucleotides of nucleotides 1-1659 of SEQ ID NO: 27; determining a test expression level of ARP12 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP12 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a blood, urine or semen sample. In a further embodiment, a method of the invention is practiced with an ARP12 nucleic acid molecule that has a length of 15 to 35 nucleotides.

There further is provided herein a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP 12 regulatory agent.

The present invention additionally provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP18 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 28; determining a test expression level of ARP18 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP18 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a sample containing prostate tissue, or, for example, with a sample of blood, urine or semen. A variety of ARP18 nucleic acid molecules are useful in the methods of the invention. In one embodiment, the invention is practiced with an ARP18 nucleic acid molecule which has a length of 15 to 35 nucleotides.

The invention also provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP18 regulatory agent.

The invention also provided herein a substantially pure ARP19 nucleic acid molecule that includes the nucleotide sequence shown as SEQ ID NO: 29. Furthermore, there is provided herein a substantially pure ARP19 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-31 or 478-644 of SEQ ID NO: 29.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a

sample from the individual with an ARP19 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 29; determining a test expression level of ARP19 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP19 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a sample containing prostate tissue, or, for example, with a sample of blood, urine or semen. A variety of ARP19 nucleic acid molecules are useful in the methods of the invention, for example, ARP19 nucleic acid molecules of 15 to 35 nucleotides in length.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP19 regulatory agent.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP21 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 30; determining a test expression level of ARP21 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP21 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in the invention include, without limitation, those containing prostate tissue as well as blood, urine and semen samples. In one embodiment, a method of the invention is practiced with

an ARP21 nucleic acid molecule having a length of 15 to 35 nucleotides.

The present invention also provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP21 regulatory agent.

The present invention also provides a substantially pure ARP22 nucleic acid molecule which includes the nucleotide sequence shown as SEQ ID NO: 31. In addition, the invention provides a substantially pure ARP22 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-73 or 447-464 of SEQ ID NO: 31.

Further provided by the present invention is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP22 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 31; determining a test expression level of ARP22 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP22 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a blood, urine or semen sample. In a further embodiment, a method of the invention is practiced with an ARP22 nucleic acid molecule that includes at least 10 contiguous nucleotides of nucleotides 1-73 or 447-464 of SEQ ID NO: 31. In yet a further embodiment, a method of the invention is

practiced with an ARP22 nucleic acid molecule having a length of 15 to 35 nucleotides.

The present invention also provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP22 regulatory agent.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP29 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 32; determining a test expression level of ARP29 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP29 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a sample of blood, urine or semen. In a further embodiment, a method of the invention is practiced with an ARP29 nucleic acid molecule which has a length of 15 to 35 nucleotides.

The invention additionally provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP29 regulatory agent.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows northern analysis of ARP7, ARp15, ARP16 and ARP21 expression in androgen stimulated

cells. "+" indicates androgen-stimulated RNA; "-" indicates androgen-starved RNA.

Figure 2 shows hybridization of an ARP7 probe to two multiple tissue northern blots (Clontech).

Figure 3 shows hybridization of an ARP15 probe to two multiple tissue northern blots (Clontech).

Figure 4 shows hybridization of an ARP21 probe to two multiple tissue northern blots (Clontech).

Figure 5 shows Western blot analysis of ARP15 protein in cell lysates from prostate cancer LNCaP cells (left lane: "LNCaP") and in serum from a prostate cancer patient (right lane: "Cap Serum").

Figure 6 shows cellular localization of ARP15. (A) LNCaP cells stained with anti-ARP15 monoclonal antibody 1R. (B) LNCaP cells stained with anti-β-integrin monoclonal antibody.

Figure 7 shows immunohistochemical staining with anti-ARP15 monoclonal antibody 1R. (A) Prostate cancer tissue section stained with anti-ARP15. (B) Normal prostate tissue section stained with anti-ARP15.

DETAILED DESCRIPTION OF THE INVENTION

This invention is directed to the discovery of androgen regulated prostate (ARP) expressed nucleic acid molecules. The androgen regulated prostate expressed nucleic acid molecules and encoded gene products are useful as diagnostic markers for neoplastic conditions and other disorders of the prostate, and, further, are targets for therapy as described further herein below.

As disclosed herein in Example I, the ARP7 cDNA is an androgen-regulated sequence. The ARP7 nucleic acid molecule, which contains 5470 nucleotides, is provided herein as SEQ ID NO: 1. Nucleotides 474 to 4967 encode a polypeptide of 1498 amino acids (SEQ ID NO: 2). As shown in Figure 1, ARP7 mRNA is dramatically up-regulated by androgen in starved LNCaP cells. As further shown in Figure 2, ARP7 is most highly expressed in the prostate with little or no detectable expression in other tissues.

As further disclosed herein, the ARP15 cDNA also is a human androgen-regulated sequence (see Figure 1). The human ARP15 nucleic acid molecule (SEQ ID NO: 3), which contains 3070 nucleotides, has an open reading frame from nucleotide 253 to 1527. The ARP15 cDNA sequence is predicted to encode a polypeptide of 425 amino acids (SEQ ID NO: 4) with at least three transmembrane domains. As shown in Figure 3, ARP15 is expressed in prostate tissue and also expressed in testis and ovary.

As further disclosed herein, the ARP16 cDNA is up-regulated by androgen in human prostate cells. The human ARP16 cDNA, shown herein as SEQ ID NO: 5, has 2161 nucleotides with an open reading frame from nucleotide 138 to 1601. Furthermore, the human ARP16 is a polypeptide of 488 amino acids (SEQ ID NO: 4) with at least eight predicted transmembrane domains. As shown in Figure 1, ARP16 mRNA is dramatically up-regulated by androgen in starved LNCaP cells.

Additional androgen regulated cDNAs also are disclosed herein. ARP8 is a human sequence up-regulated by androgen in prostate cells. The human ARP8 cDNA (SEQ ID NO: 7) contains 2096 nucleotides with an open reading frame from nucleotide 1 to 1728; the encoded human ARP8

polypeptide (SEQ ID NO: 8) has 576 amino acids. The nucleic acid sequence of another human androgen-regulated cDNA expressed in prostate, ARP9, is disclosed herein as SEQ ID NO: 9. The ARP9 nucleic acid sequence disclosed herein has 2568 nucleotides with an open reading frame from nucleotide 559 to 2232. The encoded human ARP9 polypeptide (SEQ ID NO: 10) has 558 residues and is predicted to include at least four transmembrane domains. The ARP13 cDNA also increased in response to androgen in the LNCaP cell line. The ARP13 nucleotide sequence (SEQ ID NO: 11) has 2920 nucleotides with an open reading frame from nucleotide 141 to 1022. The human ARP13 polypeptide has the 294 amino acid sequence shown herein as SEQ ID NO: 12 and is predicted to include at least one transmembrane domain. The ARP20 nucleotide sequence shown herein as SEQ ID NO: 13 also was identified as positively regulated in response to androgen in LNCaP cells. The human ARP20 nucleotide sequence has 1095 nucleotides with an open reading frame from nucleotide 113 to 661; the human ARP20 polypeptide is shown herein as SEQ ID NO: 14.

As further disclosed herein, ARP24, ARP26, ARP28, ARP30, ARP33 and ARP11 also are androgen regulated cDNAs expressed in the LNCaP prostate cell line. The ARP24 cDNA sequence shown herein as SEQ ID NO: 15 contains 3007 nucleotides with an open reading frame from nucleotide 38 to 1378; the encoded human ARP24 polypeptide (SEQ ID NO: 16) has 447 amino acids predicted to encode at least four transmembrane domains. The ARP26 cDNA sequence shown herein as SEQ ID NO: 17 is a sequence of 3937 nucleotides with an open reading frame from nucleotide 240 to 1013. The corresponding androgen-regulated human ARP26 polypeptide (SEQ ID NO: 18) has 258 residues. Furthermore, the ARP28 cDNA sequence, shown herein as SEQ ID NO: 19, is a sequence of

1401 nucleotides with an open reading frame from nucleotide 45 to 1085 and is predicted to encode the 347 amino acid human ARP28 polypeptide (SEQ ID NO: 20) with at least three transmembrane domains. The androgen-regulated cDNA ARP30 has a sequence (SEQ ID NO: 21) of 3318 nucleotides; the human ARP30 polypeptide (SEQ ID NO: 22), a protein of 601 amino acids, is encoded by an open reading frame positioned at nucleotides 252 to 2054 of SEQ ID NO: 21. As further disclosed herein, the androgen-regulated ARP33 cDNA has a nucleic acid sequence (SEQ ID NO: 23) of 1690 nucleotides with an open reading frame from nucleotide 98 to 1313. The human ARP33 polypeptide, a protein of 405 residues shown herein as SEQ ID NO: 24, is predicted to include at least one transmembrane domain. In addition, the human ARP11 cDNA has a nucleic acid sequence (SEQ ID NO: 33) of 3067 nucleotides with an open reading frame from nucleotides 790 to 1805 that encodes the human ARP11 polypeptide disclosed herein as SEQ ID NO: 34.

As further disclosed herein, ARP6, ARP10, ARP12, ARP18, ARP19, ARP21, ARP22 and ARP29 also are androgen-regulated sequences expressed in prostate cells. The human ARP6 cDNA sequence is shown herein as a 504 nucleotide sequence (SEQ ID NO: 25); the human ARP10 cDNA sequence is shown herein as a 2189 nucleotide sequence (SEQ ID NO: 26); the human ARP12 cDNA sequence is shown herein as a 2576 nucleotide sequence (SEQ ID NO: 27); and the human ARP18 cDNA sequence is shown herein as a 521 nucleotide sequence (SEQ ID NO: 28). Furthermore, the human ARP19 cDNA sequence is shown herein as a 644 nucleotide sequence (SEQ ID NO: 29); the human ARP21 cDNA sequence is shown herein as a 1460 nucleotide sequence (SEQ ID NO: 30); the human ARP22 cDNA sequence is shown herein as a 774 nucleotide sequence (SEQ ID NO: 31); and

the human ARP29 cDNA sequence is shown herein as a 386 nucleotide sequence (SEQ ID NO: 32).

Based on these novel prostate-expressed sequences, the invention provides methods for diagnosing prostate neoplastic conditions. An ARP nucleic acid molecule or polypeptide of the invention can be used alone or in combination with other molecules as a specific marker for prostate cells or prostate neoplastic conditions.

The present invention provides a substantially pure ARP7 nucleic acid molecule which includes the nucleotide sequence shown as SEQ ID NO: 1. The invention also provides a substantially pure ARP7 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-445 of SEQ ID NO: 1.

The present invention also provides a substantially pure ARP15 nucleic acid molecule that includes the nucleotide sequence shown as SEQ ID NO: 3. In addition, the invention provides a substantially pure ARP15 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-86 of SEQ ID NO: 3.

The present invention additionally provides a substantially pure ARP16 nucleic acid molecule that contains a nucleic acid sequence encoding an ARP16 polypeptide having at least 90% amino acid identity with SEQ ID NO: 6. Such a nucleic acid molecule can encode, for example, the amino acid sequence shown as SEQ ID NO:6. In one embodiment, an ARP16 nucleic acid molecule of the invention includes the nucleotide sequence shown as SEQ ID NO:5. Further provided by the invention is a substantially pure ARP16 nucleic acid molecule that

includes at least 10 contiguous nucleotides of nucleotides 1-1531 of SEQ ID NO: 5.

Also provided herein is a substantially pure ARP8 nucleic acid molecule that contains a nucleic acid sequence encoding an ARP8 polypeptide having at least 65% amino acid identity with SEQ ID NO: 8. Such a substantially pure ARP8 nucleic acid molecule can encode, for example, the amino acid sequence shown as SEQ ID NO: 8. In one embodiment, an ARP8 nucleic acid molecule of the invention has the nucleotide sequence shown as SEQ ID NO: 7. Also provided herein is a substantially pure ARP8 nucleic acid molecule which includes at least 10 contiguous nucleotides of nucleotides 1-349 of SEQ ID NO: 7.

The present invention further provides a substantially pure ARP9 nucleic acid molecule that includes a nucleic acid sequence encoding an ARP9 polypeptide having at least 65% amino acid identity with SEQ ID NO: 10. A substantially pure ARP9 nucleic acid molecule of the invention can encode, for example, the amino acid sequence shown as SEQ ID NO: 10. In one embodiment, an ARP9 nucleic acid molecule includes the nucleotide sequence shown as SEQ ID NO:9. The invention also provides a substantially pure ARP9 nucleic acid molecule that includes at least 10 contiguous nucleotides of nucleotides 697-745 of SEQ ID NO: 9.

The present invention also provides a substantially pure ARP13 nucleic acid molecule that includes a nucleic acid sequence encoding an ARP13 polypeptide having at least 90% amino acid identity with SEQ ID NO: 12. Such a substantially pure ARP13 nucleic acid molecule can encode, for example, the amino acid sequence shown as SEQ ID NO: 12. In one embodiment, a

substantially pure ARP13 nucleic acid molecule of the invention has the nucleotide sequence shown as SEQ ID NO: 11.

The present invention further provides a substantially pure ARP26 nucleic acid which includes the nucleotide sequence shown as SEQ ID NO: 17. The invention also provides a substantially pure ARP26 nucleic acid molecule of the invention that includes at least 10 contiguous nucleotides of nucleotides 1404-1516 of SEQ ID NO: 17.

Further provided herein is a substantially pure ARP30 nucleic acid molecule that includes a nucleic acid sequence encoding an ARP30 polypeptide having at least 30% amino acid identity with SEQ ID NO: 22. A substantially pure ARP30 nucleic acid molecule of the invention can encode, for example, the amino acid sequence shown as SEQ ID NO: 22, and, in one embodiment, includes the nucleotide sequence shown as SEQ ID NO: 21. Also provided herein is a substantially pure ARP30 nucleic acid molecule that includes at least 10 contiguous nucleotides of nucleotides 1-132, nucleotides 832-1696, or nucleotides 2346-2796 of SEQ ID NO: 21.

The present invention also provides a substantially pure ARP11 nucleic acid molecule that contains the nucleotide sequence shown as SEQ ID NO: 33. In addition, there is provided a substantially pure ARP11 nucleic acid molecule which contains at least 10 contiguous nucleotides of nucleotides 1-458 of SEQ ID NO: 33.

The invention also provides a substantially pure ARP6 nucleic acid molecule that includes the nucleotide sequence shown as SEQ ID NO: 25. Further

provided herein is a substantially pure ARP6 nucleic acid molecule that contains at least 10 contiguous nucleotides of nucleotides 505-526 of SEQ ID NO: 25.

The present invention further provides a substantially pure ARP12 nucleic acid molecule that contains the nucleotide sequence shown as SEQ ID NO: 27. In addition, the invention provides a substantially pure ARP12 nucleic acid molecule that contains at least 10 contiguous nucleotides of nucleotides 1635-1659 of SEQ ID NO: 27.

The invention also provides a substantially pure ARP19 nucleic acid molecule that includes the nucleotide sequence shown as SEQ ID NO: 29. Furthermore, there is provided herein a substantially pure ARP19 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-31 or 478-644 of SEQ ID NO: 29.

In addition, the present invention provides a substantially pure ARP22 nucleic acid molecule which includes the nucleotide sequence shown as SEQ ID NO: 31. In addition, the invention provides a substantially pure ARP22 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-73 or 447-464 of SEQ ID NO: 31.

The nucleic acid molecules of the invention corresponding to unique sequences are useful in a variety of diagnostic procedures which employ probe hybridization methods. One advantage of employing nucleic acid hybridization in diagnostic procedures is that very small amounts of sample can be used because the analyte nucleic acid molecule can be amplified to many copies by, for example, polymerase chain reaction (PCR) or other well

known methods for nucleic acid molecule amplification and synthesis.

As used herein, the term "nucleic acid molecule" means a single- or double-stranded DNA or RNA molecule including, for example, genomic DNA, cDNA and mRNA. The term is intended to include nucleic acid molecules of both synthetic and natural origin. A nucleic acid molecule of natural origin can be derived from any animal, such as a human, non-human primate, mouse, rat, rabbit, bovine, porcine, ovine, canine, feline, or amphibian, or from a lower eukaryote. A nucleic acid molecule of the invention can be of linear, circular or branched configuration, and can represent either the sense or antisense strand, or both, of a native nucleic acid molecule. A nucleic acid molecule of the invention can further incorporate a detectable moiety such as a radiolabel, a fluorochrome, a ferromagnetic substance, a luminescent tag or a detectable moiety such as biotin.

As used herein, the term "substantially pure nucleic acid molecule" means a nucleic acid molecule that is substantially free from cellular components or other contaminants that are not the desired molecule. A substantially pure nucleic acid molecule can also be sufficiently homogeneous so as to resolve as a band by gel electrophoresis, and generate a nucleotide sequence profile consistent with a predominant species.

In particular embodiments, the present invention provides a substantially pure ARP7 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-445 of SEQ ID NO: 1; a substantially pure ARP15 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-86 of SEQ ID

NO: 3; a substantially pure ARP16 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-1531 of SEQ ID NO: 5; a substantially pure ARP8 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-349 of SEQ ID NO: 7; a substantially pure ARP9 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 697-745 of SEQ ID NO: 9; a substantially pure ARP26 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1404-1516 of SEQ ID NO: 17; a substantially pure ARP30 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-132, at least 10 contiguous nucleotides of nucleotides 832-1696, or at least 10 contiguous nucleotides of nucleotides 2346-2796 of SEQ ID NO: 21; and a substantially pure ARP11 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-458 of SEQ ID NO: 33.

The invention also provides a substantially pure ARP6 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 505-526 of SEQ ID NO: 25; a substantially pure ARP12 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1635-1659 of SEQ ID NO: 27; a substantially pure ARP19 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-31 or at least 10 contiguous nucleotides of nucleotides 478-644 of SEQ ID NO: 29; and a substantially pure ARP22 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-73 or at least 10 contiguous nucleotides of nucleotides 447-464 of SEQ ID NO: 31.

Such a nucleic acid molecule having "at least 10 contiguous nucleotides" is a portion of a full-length nucleic acid molecule having the ability to selectively

hybridize with the parent nucleic acid molecule. As used herein, the term "selectively hybridize" means an ability to bind the parent nucleic acid molecule without substantial cross-reactivity with a molecule that is not the parent nucleic acid molecule. Therefore, the term selectively hybridize includes specific hybridization where there is little or no detectable cross-reactivity with other nucleic acid molecules. The term also includes minor cross-reactivity with other molecules provided hybridization to the parent nucleic acid molecule is distinguishable from hybridization to the cross-reactive species. Thus, a nucleic acid molecule of the invention can be used, for example, as a PCR primer to selectively amplify a parent nucleic acid molecule; as a selective primer for 5' or 3' RACE to determine additional 5' or 3' sequence of a parent nucleic acid molecule; as a selective probe to identify or isolate a parent nucleic acid molecule on a RNA or DNA blot, or within a genomic or cDNA library; or as a selective inhibitor of transcription or translation of an ARP in a tissue, cell or cell extract.

A nucleic acid molecule of the invention includes at least 10 contiguous nucleotides corresponding to the reference nucleic acid molecule, and can include at least 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45 or 50 nucleotides and, if desired, can include at least 100, 200, 300, 400, 500 or 1000 nucleotides or up to the full length of the reference nucleic acid molecule. Nucleic acid molecules of such lengths are able to selectively hybridize with the subject nucleic acid molecule in a variety of detection formats described herein.

As used herein, the term "substantially the nucleotide sequence" in reference to a nucleic acid

molecule or nucleic acid probe of the invention includes sequences having one or more additions, deletions or substitutions with respect to the reference sequence, so long as the nucleic acid molecule retains its ability to selectively hybridize with the subject nucleic acid molecule.

Nucleic acid molecules of the invention are useful, in part, as hybridization probes in diagnostic procedures. The nucleic acid molecules can be as long as the full length transcript or as short as about 10 to 15 nucleotides, for example, 15 to 18 nucleotides in length. A nucleic acid molecule of the invention that is not a full-length sequence can correspond to a coding region or an untranslated region. The particular application and degree of desired specificity will be one consideration well known to those skilled in the art in selecting a nucleic acid molecule for a particular application. For example, if it is desired to detect an ARP and other related species, the probe can correspond to a coding sequence and be used in low stringency hybridization conditions. Alternatively, using high stringency conditions with a probe of the invention will select a specific ARP7, ARP15, ARP16, ARP8, ARP9, ARP13, ARP26, ARP30, ARP11, ARP6, ARP12, ARP19 or ARP22 nucleic acid molecule. Untranslated region sequences corresponding to an ARP transcript also can be used to construct probes since there is little evolutionary pressure to conserve non-coding domains. Nucleic acid molecules as small as 15 nucleotides are statistically unique sequences within the human genome. Therefore, fragments of 15 nucleotides or more of the ARP sequences disclosed herein as SEQ ID NOS: 1, 3, 5, 7, 9, 11, 17, 21, 25, 27, 29, 31 and 33 can be constructed from essentially any region of an ARP cDNA, mRNA or promoter/regulatory region and be capable of uniquely hybridizing to ARP DNA or RNA.

A nucleic acid molecule of the invention can be produced recombinantly or chemically synthesized using methods well known in the art. Additionally, an ARP nucleic acid molecule can be labeled with a variety of detectable labels including, for example, radioisotopes, fluorescent tags, reporter enzymes, biotin and other ligands for use as a probe in a hybridization method. Such detectable labels can additionally be coupled with, for example, colorimetric or photometric indicator substrate for spectrophotometric detection. Methods for labeling and detecting nucleic acid molecules are well known in the art and can be found described in, for example, Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Press, Plainview, New York (1989), and Ausubel et al., Current Protocols in Molecular Biology (Supplement 47), John Wiley & Sons, New York (1999).

The nucleic acid molecules of the invention can be hybridized under various stringency conditions readily determined by one skilled in the art. Depending on the particular assay, one skilled in the art can readily vary the stringency conditions to optimize detection of an ARP nucleic acid molecule.

In general, the stability of a hybrid is a function of the ion concentration and temperature. Typically, a hybridization reaction is performed under conditions of lower stringency, followed by washes of varying, but higher, stringency. Moderately stringent hybridization refers to conditions that permit a nucleic acid molecule such as a probe to bind a complementary nucleic acid molecule. The hybridized nucleic acid molecules generally have at least 60% identity, at least 75% identity, at least 85% identity; or at least 90% identity with the parent or target nucleic acid sequence.

Moderately stringent conditions are conditions equivalent to hybridization in 50% formamide, 5X Denhardt's solution, 5X SSPE, 0.2% SDS at 42°C, followed by washing in 0.2X SSPE, 0.2% SDS, at 42°C. High stringency conditions can be provided, for example, by hybridization in 50% formamide, 5X Denhart's solution, 5X SSPE, 0.2% SDS at 42°C, followed by washing in 0.1X SSPE, and 0.1% SDS at 65°C.

The term low stringency hybridization means conditions equivalent to hybridization in 10% formamide, 5X Denhart's solution, 6X SSPE, 0.2% SDS at 22°C, followed by washing in 1X SSPE, 0.2% SDS, at 37°C. Denhart's solution contains 1% Ficoll, 1% polyvinylpyrolidine, and 1% bovine serum albumin (BSA). 20X SSPE (sodium chloride, sodium phosphate, ethylene diamide tetraacetic acid (EDTA)) contains 3M sodium chloride, 0.2M sodium phosphate, and 0.025 M (EDTA). Other suitable moderate stringency and high stringency hybridization buffers and conditions are well known to those of skill in the art and are described, for example, in Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Press, Plainview, New York (1989); and Ausubel et al., *supra*, 1999). Nucleic acid molecules encoding polypeptides hybridize under moderately stringent or high stringency conditions to substantially the entire sequence, or substantial portions, for example, typically at least 15-30 nucleotides of an ARP nucleic acid sequence.

The invention also provides a modification of an ARP nucleotide sequence that hybridizes under moderately stringent conditions to an ARP nucleic acid molecule, for example, an ARP nucleic acid molecule referenced herein as SEQ ID NO: 1, 3, 5, 7, 9, 11, 17, 21, 25, 27, 29, 31 or 33. Modifications of ARP

nucleotide sequences, where the modification has at least 60% identity to an ARP nucleotide sequence, are also provided. The invention also provides modification of an ARP nucleotide sequence having at least 65% identity, at least 70% identity, at least 75% identity, at least 80% identity, at least 85% identity, at least 90% identity, or at least 95% identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 17, 21, 25, 27, 29, 31 or 33.

Identity of any two nucleic acid sequences can be determined by those skilled in the art based, for example, on a BLAST 2.0 computer alignment, using default parameters. BLAST 2.0 searching is available at http://www.ncbi.nlm.nih.gov/gorf/bl2.html., as described by Tatiana et al., FEMS Microbiol Lett. 174:247-250 (1999); Altschul et al., Nucleic Acids Res., 25:3389-3402 (1997).

The present invention further provides substantially pure ARP polypeptides encoded by the prostate-expressed nucleic acid molecules of the invention. In particular, the present invention provides a substantially pure ARP16 polypeptide that contains an amino acid sequence having at least 90% amino acid identity with SEQ ID NO: 6. An ARP16 polypeptide of the invention can include, for example, the amino acid sequence shown as SEQ ID NO: 6. Also provided by the invention is a substantially pure ARP16 polypeptide fragment which has at least eight contiguous amino acids of SEQ ID NO: 6. In one embodiment, an ARP16 polypeptide fragment of the invention has at least eight contiguous amino acids of residues 1-465 of SEQ ID NO: 6.

The present invention further provides a substantially pure ARP8 polypeptide that contains an amino acid sequence having at least 65% amino acid

identity with SEQ ID NO: 8. Such an ARP8 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 8. In addition, there is provided herein a substantially pure ARP8 polypeptide fragment, which includes at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8. In one embodiment, the ARP8 fragment has at least eight contiguous amino acids of residues 249-576 of SEQ ID NO: 8.

The invention also provides a substantially pure ARP9 polypeptide that includes an amino acid sequence having at least 65% amino acid identity with SEQ ID NO: 10. Such an ARP9 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 10. Substantially pure ARP9 polypeptide fragments also are provided herein. The ARP9 fragments of the invention have at least eight contiguous amino acids of residues 1-83 of SEQ ID NO: 10. In one embodiment, such an ARP9 fragment has at least eight contiguous amino acids of residues 47-62 of SEQ ID NO: 10.

Also provided herein is a substantially pure ARP13 polypeptide, which has an amino acid sequence having at least 90% amino acid identity with SEQ ID NO: 12. As an example, a substantially pure ARP13 polypeptide of the invention can have the amino acid sequence shown as SEQ ID NO: 12. The invention additionally provides a substantially pure ARP13 polypeptide fragment that includes at least eight contiguous amino acids of SEQ ID NO: 12.

The invention also provides a substantially pure ARP20 polypeptide that includes an amino acid sequence having at least 55% amino acid identity with SEQ ID NO: 14. Such an ARP20 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 14.

Also provided herein is a substantially pure ARP20 polypeptide fragment including at least eight contiguous amino acids of SEQ ID NO: 14.

Further provided herein is a substantially pure ARP24 polypeptide that includes an amino acid sequence having at least 30% amino acid identity with SEQ ID NO: 16. A substantially pure ARP24 polypeptide of the invention can have, for example, the amino acid sequence shown as SEQ ID NO: 16. The invention also provides a substantially pure ARP24 polypeptide fragment which contains at least eight contiguous amino acids of SEQ ID NO: 16.

Also provided herein is a substantially pure ARP30 polypeptide that contains an amino acid sequence having at least 30% amino acid identity with SEQ ID NO: 22. In one embodiment, a substantially pure ARP30 polypeptide of the invention includes the amino acid sequence shown as SEQ ID NO: 22. The invention also provides a substantially pure ARP30 polypeptide fragment that has at least eight contiguous amino acids of SEQ ID NO: 22.

The invention also provides a substantially pure ARP33 polypeptide that includes an amino acid sequence having at least 70% amino acid identity with SEQ ID NO: 24. Such a substantially pure ARP33 polypeptide can have, for example, the amino acid sequence shown as SEQ ID NO: 24. Also provided herein is a substantially pure ARP33 polypeptide fragment that includes at least eight contiguous amino acids of residues 1-132 or 251-405 of SEQ ID NO: 24.

The invention further provides a substantially pure ARP11 polypeptide which contains an amino acid

sequence having at least 75% amino acid identity with SEQ ID NO: 34. Such an ARP11 polypeptide can include, for example, the amino acid sequence shown as SEQ ID NO: 34. Also provided is a substantially pure ARP11 polypeptide fragment containing at least eight contiguous amino acids of SEQ ID NO: 34.

Exemplary polypeptide fragments include those fragments having amino acids 1 to 8, 2 to 9, 3 to 10, etc., of SEQ ID NO: 6, 8, 10, 12, 14, 16, 22, 24 or 34. The invention also encompasses other polypeptide fragments which are potential antigenic fragments capable of eliciting an immune response, and thereby generating antibodies selective for an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide or polypeptide fragment of the invention. It is understood that polypeptide fragments of other lengths also can be useful, for example, a polypeptide having at least nine, ten, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45 or more contiguous amino acids of the amino acid sequence disclosed herein as SEQ ID NO: 6, residues 1-465 of SEQ ID NO: 6; residues 1-116 of SEQ ID NO: 8; residues 249-576 of SEQ ID NO: 8; residues 1-83 of SEQ ID NO: 10; residues 47-62 of SEQ ID NO: 10; the amino acid sequence disclosed herein as SEQ ID NO: 12; the amino acid sequence disclosed herein as SEQ ID NO: 14; the amino acid sequence disclosed herein as SEQ ID NO: 16; the amino acid sequence disclosed herein as SEQ ID NO: 22; residues 1-132 of the amino acid sequence disclosed herein as SEQ ID NO: 24; residues 251-405 of the amino acid sequence disclosed herein as SEQ ID NO: 24; or the amino acid sequence disclosed herein as SEQ ID NO: 34. It is understood that polypeptide fragments encompassed by the invention further include, for example, polypeptide fragments having at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600,

650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1110, 1150, 1200, 1250, 1300, 1350, 1400, 1450 or 1500 amino acids beginning at residue 1, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1110, 1150, 1200, 1250, 1300, 1350, 1400, 1450 of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 22, SEQ ID NO: 24 or SEQ ID NO: 34. Such polypeptide fragments can be useful to produce binding agents or in any of the compositions or diagnostic or therapeutic methods of the invention.

The term "ARP16 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP16 (SEQ ID NO: 6) and that has at least one biological activity of human ARP16. Such an ARP16 polypeptide has 90% or more amino acid sequence identity to SEQ ID NO:16 and can have, for example, 92%, 94%, 96%, 98%, 99% or more sequence identity to human ARP16 (SEQ ID NO: 6). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., Nucleic Acids Res. 22:4673-4680 (1994)).

Thus, it is clear to the skilled person that the term "ARP16 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 6, provided that the peptide has at least 90% amino acid identity with SEQ ID NO: 6 and retains at least one biological activity of human ARP16. An ARP16 polypeptide can be, for example, a naturally occurring variant of human ARP16 (SEQ ID NO: 6); a species homolog such as a porcine, bovine or primate homolog; an ARP16 polypeptide mutated by recombinant techniques, and the like. In view of the above definition, it is clear to the skilled person that

the mouse protein shown in Genbank accession BAB28556, which shares 87% amino acid identity with human ARP16 (SEQ ID NO: 6), is not encompassed by the invention.

The term "ARP8 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP8 (SEQ ID NO: 8) and that has at least one biological activity of human ARP8. Such an ARP8 polypeptide has 65% or more amino acid sequence identity to SEQ ID NO:5 and can have, for example 70%, 75%, 80%, 85%, 90%, 95% or more amino acid sequence identity to human ARP8 (SEQ ID NO: 8). Percent amino acid identity can be determined using Clustal W version 1.7 as described above.

Thus, the term "ARP8 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO:8, provided that the peptide has at least 65% amino acid identity with SEQ ID NO: 8 and retains at least one biological activity of human ARP8. An ARP8 polypeptide can be, for example, a naturally occurring variant of human ARP8 (SEQ ID NO: 8); a species homolog such as a non-mammalian or mammalian homolog, for example, a murine, bovine or primate homolog; an ARP8 polypeptide mutated by recombinant techniques; and the like. The polypeptide encoded by murine protein (Genbank accession BAB28455), which shares 62% amino acid identity with human ARP8 (SEQ ID NO: 8), is not encompassed by the invention.

The term "ARP9 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP9 (SEQ ID NO: 10) and that has at least one biological activity of human ARP9. Such an ARP9

polypeptide has 65% or more amino acid sequence identity to SEQ ID NO: 10 and can have, for example, 70%, 75%, 80%, 85%, 90%, 95% or more amino acid sequence identity to human ARP9 (SEQ ID NO: 10). Percent amino acid identity can be determined using Clustal W version 1.7 as described above.

Thus, the term "ARP9 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 10, provided that the peptide has at least 65% amino acid identity with SEQ ID NO: 10 and retains at least one biological activity of human ARP9. An ARP9 polypeptide can be, for example, a naturally occurring variant of human ARP9 (SEQ ID NO: 10); a species homolog such as a non-mammalian or mammalian homolog, for example, a murine, bovine or primate homolog; an ARP9 polypeptide mutated by recombinant techniques; and the like. The polypeptide encoded by Genbank accession NP_071769), which shares 63% amino acid identity with human ARP9 (SEQ ID NO: 10), is not encompassed by the invention.

The term "ARP13 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP13 (SEQ ID NO: 12) and that has at least one biological activity of human ARP13. Such an ARP13 polypeptide has 90% or more amino acid sequence identity to SEQ ID NO:12 and can have, for example, 92%, 94%, 96%, 98%, 99% or more sequence identity to human ARP13 (SEQ ID NO: 12). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., *supra*, 1994).

The term "ARP13 polypeptide" encompasses polypeptides with one or more naturally occurring or

non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 12, provided that the peptide has at least 90% amino acid identity with SEQ ID NO: 12 and retains at least one biological activity of human ARP13. An ARP13 polypeptide can be, for example, a naturally occurring variant of human ARP13 (SEQ ID NO: 12); a species homolog such as a non-mammalian or mammalian homolog, for example, a murine, bovine or primate homolog; an ARP13 polypeptide mutated by recombinant techniques, and the like. In view of the above definition, it is clear to the skilled person that the polypeptide encoded by Genbank accession BAB29190, which shares 86% amino acid identity with human ARP13 (SEQ ID NO: 12), is not encompassed by the invention.

The term "ARP20 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP20 (SEQ ID NO: 14) and that has at least one biological activity of human ARP20. Such an ARP20 polypeptide has 55% or more amino acid sequence identity to SEQ ID NO:12 and can have, for example, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more sequence identity to human ARP20 (SEQ ID NO: 14). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., *supra,* 1994).

The term "ARP20 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 14, provided that the peptide has at least 55% amino acid identity with SEQ ID NO: 14 and retains at least one biological activity of human ARP20. An ARP20 polypeptide can be, for example, a naturally occurring variant of human ARP20 (SEQ ID NO: 14); a species homolog such as a

non-mammalian or mammalian homolog, for example, a murine, bovine or primate homolog; an ARP20 polypeptide mutated by recombinant techniques, and the like. In view of the above definition, it is clear to the skilled person that the polypeptide encoded by Genbank accession AAL27184, which shares 50% amino acid identity with human ARP20 (SEQ ID NO: 14), is not encompassed by the invention.

The term "ARP24 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP24 (SEQ ID NO: 16) and that has at least one biological activity of human ARP24. Such an ARP24 polypeptide has 30% or more amino acid sequence identity to SEQ ID NO:14 and can have, for example, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more sequence identity to human ARP24 (SEQ ID NO: 16). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., *supra,* 1994).

The term "ARP24 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 16, provided that the peptide has at least 30% amino acid identity with SEQ ID NO: 16 and retains at least one biological activity of human ARP24. An ARP24 polypeptide can be, for example, a naturally occurring variant of human ARP24 (SEQ ID NO: 16); a species homolog such as a non-mammalian or mammalian homolog, for example, a murine, bovine or primate homolog; an ARP24 polypeptide mutated by recombinant techniques, and the like.

Similarly, the term "ARP30 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP30 (SEQ ID NO: 22) and that has at least

one biological activity of human ARP30. Such an ARP30 polypeptide has 30% or more amino acid sequence identity to SEQ ID NO:20 and can have, for example, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more sequence identity to human ARP30 (SEQ ID NO: 22). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., *supra,* 1994).

The term "ARP30 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 22, provided that the peptide has at least 30% amino acid identity with SEQ ID NO: 22 and retains at least one biological activity of human ARP30. An ARP30 polypeptide can be, for example, a naturally occurring variant of human ARP30 (SEQ ID NO: 22); a species homolog such as a non-mammalian or mammalian homolog, for example, a murine, bovine or primate homolog; an ARP30 polypeptide mutated by recombinant techniques, and the like.

The term "ARP33 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP33 (SEQ ID NO: 24) and that has at least one biological activity of human ARP33. Such an ARP33 polypeptide has 70% or more amino acid sequence identity to SEQ ID NO:22 and can have, for example, 75%, 80%, 85%, 90%, 95% or more sequence identity to human ARP33 (SEQ ID NO: 24). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., *supra,* 1994).

The term "ARP33 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 24,

provided that the peptide has at least 70% amino acid identity with SEQ ID NO: 24 and retains at least one biological activity of human ARP33. An ARP33 polypeptide can be, for example, a naturally occurring variant of human ARP33 (SEQ ID NO: 24); a species homolog including mammalian and non-mammalian homologs and murine, bovine, and primate homologs; an ARP33 polypeptide mutated by recombinant techniques, and the like. In view of the above, it is understood that the murine polypeptide encoded by Genbank accession NP_033387, which shares 67% amino acid identity with human ARP33 (SEQ ID NO: 24), is not encompassed by the invention.

The term "ARP11 polypeptide" as used herein, means a polypeptide that is structurally similar to a human ARP11 (SEQ ID NO: 34) and that has at least one biological activity of human ARP11. Such an ARP11 polypeptide has 75% or more amino acid sequence identity to SEQ ID NO: 34 and can have, for example, 80%, 85%, 90%, 95% or more sequence identity to human ARP11 (SEQ ID NO: 34). Percent amino acid identity can be determined using Clustal W version 1.7 (Thompson et al., Nucleic Acids Res. 22:4673-4680 (1994)).

Thus, it is clear to the skilled person that the term "ARP11 polypeptide" encompasses polypeptides with one or more naturally occurring or non-naturally occurring amino acid substitutions, deletions or insertions as compared to SEQ ID NO: 34, provided that the peptide has at least 75% amino acid identity with SEQ ID NO: 34 and retains at least one biological activity of human ARP11. An ARP11 polypeptide can be, for example, a naturally occurring variant of human ARP11 (SEQ ID NO: 34); a species homolog such as a porcine, bovine or primate homolog; an ARP11 polypeptide mutated by recombinant techniques, and the like. In view of the

above definition, it is clear to the skilled person that the mouse protein shown in Genbank accession BAB28028, which shares 72% amino acid identity with human ARP11 (SEQ ID NO: 34), is not encompassed by the invention.

Modifications to the ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 and ARP11 polypeptides of SEQ ID NOS: 6, 8, 10, 12, 14, 16, 22, 24 and 34 that are encompassed within the invention include, for example, an addition, deletion, or substitution of one or more conservative or non-conservative amino acid residues; substitution of a compound that mimics amino acid structure or function; or addition of chemical moieties such as amino or acetyl groups.

The present invention also provides a variety of binding agents that selectively bind an ARP polypeptide of the invention. Such binding agents encompass, but are not limited to, polyclonal and monoclonal antibodies and binding portions thereof.

The present invention provides an ARP16 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 6. In one embodiment, such an ARP16 binding agent selectively binds at least eight contiguous amino acids of residues 1-465 of SEQ ID NO: 6. In another embodiment, the binding agent is an antibody.

Also provided herein is an ARP8 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8, for example, an antibody that selectively binds at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8. In addition, the invention provides a binding agent which includes a molecule that selectively

binds at least eight contiguous amino acids of residues 249-576 of SEQ ID NO: 8. Such an ARP8 binding agent can be, for example, an antibody.

The invention also provides an ARP9 binding agent that includes a molecule that selectively binds at least eight contiguous amino acids of residues 1-83 of SEQ ID NO: 10. In one embodiment, the ARP9 binding agent includes a molecule that selectively binds at least eight contiguous amino acids of residues 47-62 of SEQ ID NO: 10. An ARP9 binding agent of the invention can be, for example, an antibody.

Further provided herein is an ARP13 binding agent which includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 12. ARP13 binding agents include, without limitation, antibodies.

The invention also provides an ARP20 binding agent which contains a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 14. In one embodiment, the ARP20 binding agent is an antibody.

In addition, there is provided herein an ARP24 binding agent that includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 16. In one embodiment, the ARP24 binding agent is an antibody.

In addition, there is provided herein an ARP30 binding agent, which includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 22. ARP30 binding agents encompass but are not limited to antibodies.

The present invention also provides an ARP33 binding agent that includes a molecule that selectively binds at least eight contiguous amino acids of residues 1-132 or at least eight contiguous amino acids of 251-405 of SEQ ID NO: 24. In a particular embodiment, the ARP33 binding agent is an antibody.

Further provided herein is an ARP11 binding agent, which includes a molecule that selectively binds at least eight contiguous amino acids of SEQ ID NO: 34. ARP11 binding agents encompass, but are not limited to, antibodies.

As used herein, the term "binding agent" when used in reference to a specified ARP polypeptide, means a compound, including a simple or complex organic molecule, a metal containing compound, carbohydrate, peptide, protein, peptidomimetic, glycoprotein, lipoprotein, lipid, nucleic acid molecule, antibody, or the like that selectively binds an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide, or the specified fragment thereof. For example, a binding agent can be a polypeptide that selectively binds with high affinity or avidity to the specified ARP polypeptide, without substantial cross-reactivity to other unrelated polypeptides. The affinity of a binding agent that selectively binds an ARP polypeptide generally is greater than about 10^5 M^{-1} and can be greater than about 10^6 M^{-1}. A binding agent also can bind with high affinity; such an agent generally binds with an affinity greater than 10^8 M^{-1} to 10^9 M^{-1}. Specific examples of such selective binding agents include a polyclonal or monoclonal antibody selective for an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide, or the specified fragment thereof; or a nucleic acid molecule, nucleic acid analog, or small organic molecule,

identified, for example, by affinity screening of the appropriate library. For certain applications, a binding agent can be utilized that preferentially recognizes a particular conformational or post-translationally modified state of the specified ARP polypeptide. The binding agent can be labeled with a detectable moiety, if desired, or rendered detectable by specific binding to a detectable secondary binding agent.

As used herein, the term "antibody" is used in its broadest sense to mean polyclonal and monoclonal antibodies, including antigen binding fragments of such antibodies. As used herein, the term antigen means a native or synthesized fragment of a polypeptide of the invention. Such an antibody of the invention, or antigen binding fragment of such an antibody, is characterized by having specific binding activity for an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33, or ARP11 polypeptide, or the specified fragment thereof, of at least about 1×10^5 M^{-1}. Thus, Fab, $F(ab')_2$, Fd and Fv fragments of an anti-ARP antibody, which retain specific binding activity for an ARP polypeptide of the invention, or fragment thereof, are included within the definition of an antibody. Specific binding activity can be readily determined by one skilled in the art, for example, by comparing the binding activity of the antibody to the specified ARP polypeptide, or fragment thereof, versus a control polypeptide that does not include a polypeptide of the invention. Methods of preparing polyclonal or monoclonal antibodies are well known to those skilled in the art (see, for example, Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1988)).

The term "antibody" also includes naturally occurring antibodies as well as non-naturally occurring

antibodies, including, for example, single chain antibodies, chimeric, bi-functional and humanized antibodies, as well as antigen-binding fragments thereof. Such non-naturally occurring antibodies can be constructed using solid phase peptide synthesis, produced recombinantly or obtained, for example, by screening combinatorial libraries consisting of variable heavy chains and variable light chains as described by Huse et al. (Science 246:1275-1281 (1989)). These and other methods of making, for example, chimeric, humanized, CDR-grafted, single chain, and bi-functional antibodies are well known to those skilled in the art (Winter and Harris, Immunol. Today 14:243-246 (1993); Ward et al., Nature 341:544-546 (1989) ; Harlow and Lane, *supra*, 1988); Hilyard et al., Protein Engineering: A practical approach (IRL Press 1992); Borrabeck, Antibody Engineering, 2d ed. (Oxford University Press 1995)).

An antibody of the invention can be prepared using as an immunogen an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide, which can be prepared from natural sources or produced recombinantly, or a polypeptide fragment containing at least 8 contiguous amino acids of SEQ ID NO: 6, at least 8 contiguous amino acids of residues 1-116 or 249-576 of SEQ ID NO: 8; at least 8 contiguous amino acids of residues 1-83 or 47-62 of SEQ ID NO: 10; at least 8 contiguous amino acids of SEQ ID NO: 12, 14, 16 or 22; at least 8 contiguous amino acids of residues 1-132 of SEQ ID NO: 24; at least 8 contiguous amino acids of residues 251-405 of SEQ ID NO: 24; or at least 8 contiguous amino acids of SEQ ID NO: 34. Such polypeptide fragments are functional antigenic fragments if the antigenic peptides can be used to generate an antibody selective for an ARP polypeptide of the invention. As is well known in the art, a non-immunogenic or weakly immunogenic ARP

polypeptide of the invention, or polypeptide fragment thereof, can be made immunogenic by coupling the hapten to a carrier molecule such as bovine serum albumin (BSA) or keyhole limpet hemocyanin (KLH). Various other carrier molecules and methods for coupling a hapten to a carrier molecule are well known in the art (see, for example, Harlow and Lane, *supra*, 1988). An immunogenic ARP polypeptide fragment of the invention can also be generated by expressing the peptide portion as a fusion protein, for example, to glutathione S transferase (GST), polyHis or the like. Methods for expressing peptide fusions are well known to those skilled in the art (Ausubel et al., Current Protocols in Molecular Biology (Supplement 47), John Wiley & Sons, New York (1999)).

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method is practiced by contacting a sample from the individual with an ARP7 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 1; determining a test expression level of ARP7 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP7 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a prostate tissue sample. In another embodiment, the method is practiced with a sample of blood, urine or semen. In a further embodiment, the method is practiced with an ARP7 nucleic acid molecule that has a length of 15 to 35 nucleotides. In yet a further embodiment, the invention is practiced with an ARP7 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-445 of SEQ ID NO: 1.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP15 nucleic acid molecule that includes at least 10 contiguous nucleotides of SEQ ID NO: 3; determining a test expression level of ARP15 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP15 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A sample useful in such a method of the invention can include, for example, prostate tissue, or can be, for example, blood, urine or semen. An ARP15 nucleic acid molecule useful in a method of the invention can have a length of, for example, 15 to 35 nucleotides. In one embodiment, the ARP15 nucleic acid molecule has at least 10 contiguous nucleotides of nucleotides 1-86 of SEQ ID NO: 3.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP16 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 5; determining a test expression level of ARP16 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP16 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in the methods of the invention include, for example, prostate tissue samples as well as samples of blood, urine or semen. In one embodiment, a method of the invention is practiced with an ARP16 nucleic acid molecule which has a length of 15

to 35 nucleotides. In another embodiment, a method of the invention is practiced with an ARP16 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-1531 of SEQ ID NO: 5.

The invention additionally provides method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP8 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO:7; determining a test expression level of ARP8 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP8 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the sample includes prostate tissue. In other embodiments, the sample is blood, urine or semen. In a further embodiment, the ARP8 nucleic acid molecule has a length of 15 to 35 nucleotides. In yet a further embodiment, the ARP8 nucleic acid molecule includes at least 10 contiguous nucleotides of nucleotides 1-349 of SEQ ID NO: 7.

Further provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP9 nucleic acid molecule that includes at least 10 contiguous nucleotides of SEQ ID NO: 9; determining a test expression level of ARP9 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP9 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention

is practiced with a sample that includes prostate tissue. In other embodiments, a method of the invention is practiced with a sample of blood, urine or semen. In a further embodiment, a method of the invention is practiced with an ARP9 nucleic acid molecule having a length of 15 to 35 nucleotides. In yet a further embodiment, a method of the invention is practiced with an ARP9 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 697-745 of SEQ ID NO: 9.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP13 nucleic acid molecule that includes at least 10 contiguous nucleotides of SEQ ID NO: 11; determining a test expression level of ARP13 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP13 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a sample which includes prostate tissue or, for example, with a blood, urine or semen sample. A variety of ARP13 nucleic acid molecules are useful in the methods of the invention including ARP13 nucleic acid molecules of 15 to 35 nucleotides in length.

There further is provided herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP20 nucleic acid molecule which includes at least 10 contiguous

nucleotides of SEQ ID NO: 13; determining a test expression level of ARP20 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP20 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in a method of the invention include prostate tissue, blood, urine and semen. In one embodiment, a method of the invention is practiced with an ARP20 nucleic acid molecule having a length of 15 to 35 nucleotides.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. The method includes the steps of contacting a sample from the individual with an ARP24 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 15; determining a test expression level of ARP24 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP24 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a sample containing prostate tissue. In other embodiments, a method of the invention is practiced with a sample of blood, urine or semen. In yet another embodiment, the method is practiced with an ARP24 nucleic acid molecule that is 15 to 35 nucleotides in length.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual. A method of the invention includes the steps of contacting a sample from the individual with an ARP26 nucleic acid molecule containing

at least 10 contiguous nucleotides of SEQ ID NO: 17; determining a test expression level of ARP26 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP26 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in a method of the invention include prostate tissue, blood, urine and semen. In one embodiment, a method of the invention is practiced with an ARP26 nucleic acid molecule having a length of 15 to 35 nucleotides. In another embodiment, a method of the invention is practiced with an ARP26 nucleic acid molecule having at least 10 contiguous nucleotides of nucleotides 1404-1516 of SEQ ID NO: 17.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, in which a sample from the individual is contacted with an ARP28 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 19; a test expression level of ARP28 RNA in the sample is determined; and the test expression level is compared to a non-neoplastic control expression level of ARP28 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the sample contacted with an ARP28 nucleic acid molecule contains prostate tissue. In other embodiments, the sample is blood, urine or semen sample. In a further embodiment, the ARP28 nucleic acid molecule has a length of 15 to 35 nucleotides.

The invention also provides herein a method of diagnosing or predicting susceptibility to a prostate

neoplastic condition in an individual by contacting a sample from the individual with an ARP30 nucleic acid molecule containing at least 10 contiguous nucleotides of nucleotides 1-1829 or nucleotides 2346-3318 of SEQ ID NO: 21; determining a test expression level of ARP30 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP30 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a sample containing prostate tissue. In other embodiments, a method of the invention is practiced with a blood, urine or semen sample. In a further embodiment, a method of the invention is practiced with an ARP30 nucleic acid molecule having a length of 15 to 35 nucleotides. In yet a further embodiment, a method of the invention is practiced with an ARP30 nucleic acid molecule that includes at least 10 contiguous nucleotides of nucleotides 1-132, nucleotides 832-1696, or nucleotides 2346-2796 of SEQ ID NO: 21.

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP33 nucleic acid molecule that includes at least 10 contiguous nucleotides of SEQ ID NO: 23; determining a test expression level of ARP33 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP33 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in the invention can include, for example, prostate tissue. Samples useful in the invention also can be samples of blood, urine or

semen. A variety of ARP33 nucleic acid molecules are useful in the methods of the invention including, for example, ARP33 nucleic acid molecules of 15 to 35 nucleotides in length.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP11 nucleic acid molecule containing at least 10 contiguous nucleotides of nucleotides 1-458 of SEQ ID NO: 33; determining a test expression level of ARP11 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP11 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A sample useful for diagnosing or predicting susceptibility to a prostate neoplastic condition according to a method of the invention can be, for example, a sample of prostate tissue or a sample of blood, urine or semen. In one embodiment, a method of the invention is practiced with an ARP11 nucleic acid molecule having a length of 15 to 35 nucleotides.

The invention additionally provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP6 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 25; determining a test expression level of ARP6 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP6 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the

individual. In one embodiment, the method is practiced with a prostate tissue sample. In another embodiment, the method is practiced with a sample of blood, urine or semen. In a further embodiment, the method is practiced with an ARP6 nucleic acid molecule having a length of 15 to 35 nucleotides. In yet a further embodiment, the method is practiced with an ARP6 nucleic acid molecule which contains at least 10 contiguous nucleotides of nucleotides 505-526 of SEQ ID NO: 25.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP10 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 26; determining a test expression level of ARP10 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP10 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a blood, urine or semen sample. In a further embodiment, the method is practiced with an ARP10 nucleic acid molecule of 15 to 35 nucleotides in length.

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP12 nucleic acid molecule containing at least 10 contiguous nucleotides of nucleotides 1-1659 or 2176-2576 of SEQ ID NO: 27; determining a test expression level of ARP12 RNA in the sample; and comparing the test expression level to a non-

neoplastic control expression level of ARP12 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a blood, urine or semen sample. In a further embodiment, a method of the invention is practiced with an ARP12 nucleic acid molecule that has a length of 15 to 35 nucleotides. In yet a further embodiment, a method of the invention is practiced with an ARP12 nucleic acid molecule that contains at least 10 contiguous nucleotides of nucleotides 1635-1659 of SEQ ID NO: 27.

The present invention additionally provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP18 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 28; determining a test expression level of ARP18 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP18 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a sample containing prostate tissue, or, for example, with a sample of blood, urine or semen. A variety of ARP18 nucleic acid molecules are useful in the methods of the invention. In one embodiment, the invention is practiced with an ARP18 nucleic acid molecule which has a length of 15 to 35 nucleotides.

The invention further provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP19 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 29; determining a test expression level of ARP19 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP19 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a sample containing prostate tissue, or, for example, with a sample of blood, urine or semen. A variety of ARP19 nucleic acid molecules are useful in the methods of the invention, for example, ARP19 nucleic acid molecules of 15 to 35 nucleotides in length. In a particular embodiment, a method of the invention is practiced with an ARP19 nucleic acid molecule which has at least 10 contiguous nucleotides of nucleotides 1-31 or 478-644 of SEQ ID NO: 29.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP21 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 30; determining a test expression level of ARP21 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP21 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in the invention include, without limitation, those containing prostate tissue as well as blood, urine and semen samples. In one

embodiment, a method of the invention is practiced with an ARP21 nucleic acid molecule having a length of 15 to 35 nucleotides.

Further provided by the present invention is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP22 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 31; determining a test expression level of ARP22 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP22 RNA, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a blood, urine or semen sample. In a further embodiment, a method of the invention is practiced with an ARP22 nucleic acid molecule having a length of 15 to 35 nucleotides. In yet a further embodiment, a method of the invention is practiced with an ARP22 nucleic acid molecule that has at least 10 contiguous nucleotides of nucleotides 1-73 or 447-464 of SEQ ID NO: 31.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a sample from the individual with an ARP29 nucleic acid molecule containing at least 10 contiguous nucleotides of SEQ ID NO: 32; determining a test expression level of ARP29 RNA in the sample; and comparing the test expression level to a non-neoplastic control expression level of ARP29 RNA, where an altered test expression

level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, the method is practiced with a sample containing prostate tissue. In other embodiments, the method is practiced with a sample of blood, urine or semen. In a further embodiment, a method of the invention is practiced with an ARP29 nucleic acid molecule which has a length of 15 to 35 nucleotides.

In the diagnostic methods of the invention, the sample can be, for example, a prostate tissue, or can be, for example, a fluid such as blood, urine or semen. The non-neoplastic control expression level can be determined, for example, using a normal prostate cell or an androgen-dependent cell line.

As described herein, the term "prostate neoplastic condition" means a benign or malignant or metastatic prostate lesion of proliferating cells. For example, primary prostate tumors are classified into stages TX, T0, T1, T2, T3, and T4. Metastatic prostate cancer is classified into stages D1, D2, and D3. The term further includes prostate neoplasm. Each of the above conditions is encompassed within the term "prostate neoplastic condition."

As used herein, the term "sample" means any biological fluid, cell, tissue, organ or portion thereof, that includes or potentially includes an ARP nucleic acid molecule. The term sample includes materials present in an individual as well as materials obtained or derived from the individual. For example, a sample can be a histologic section of a specimen obtained by biopsy, or cells that are placed in or adapted to tissue culture. A sample further can be a subcellular fraction or extract,

or a crude or substantially pure nucleic acid molecule. A sample can be prepared by methods known in the art suitable for the particular format of the detection method.

As used herein, the term "test expression level" is used in reference to ARP RNA expression or to ARP polypeptide expression as discussed below and means the extent, amount or rate of synthesis of the specified ARP RNA or polypeptide. The amount or rate of synthesis can be determined by measuring the accumulation or synthesis of the specified ARP RNA or polypeptide, or by measuring an activity associated with a polypeptide of the invention.

As used herein, an "altered test expression level" means a test expression level that is either elevated or reduced as compared to a control expression level. One skilled in the art understands that such an elevation or reduction is not within the inherent variability of the assay and generally is an expression level that is at least two-fold elevated or reduced. An altered test expression level can be, for example, two-fold, five-fold, ten-fold, 100-fold, 200-fold, or 1000-fold increased in the extent, amount or rate of synthesis of the specified RNA or polypeptide as compared to a control expression level of the specified ARP RNA or polypeptide. An altered test expression level also can be, for example, two-fold, five-fold, ten-fold, 100-fold, 200-fold, or 1000-fold decreased in the extent, amount or rate of synthesis of the specified ARP RNA or polypeptide compared to a control expression level of the same ARP RNA or polypeptide.

As used herein, the term "non-neoplastic control expression level" means an ARP RNA expression

level or to an ARP polypeptide expression level as discussed below used as a baseline for comparison to a test expression level. For example, a suitable control expression level can be the expression level of ARP nucleic acid or polypeptide from a non-neoplastic prostate cell or a fluid sample obtained from a normal individual. Another suitable non-neoplastic control is a prostate cell line that is androgen-dependent. It is understood that ARP nucleic acid or polypeptide expression levels determined in cell lines generally are determined under androgen-depleted growth conditions which can correlate to non-neoplastic control expression levels. The response of an androgen-depleted androgen-dependent prostate cell line to androgen stimulation will be indicative of ARP nucleic acid or polypeptide expression levels in neoplastic cells. The control expression level can be determined simultaneously with one or more test samples or, alternatively, expression levels can be established for a particular type of sample and standardized to internal or external parameters such as protein or nucleic acid content, cell number or mass of tissue. Such standardized control samples can then be directly compared with results obtained from the test sample. As indicated above, an increase of two-fold or more, for example, of a test expression level of the specified ARP nucleic acid or polypeptide indicates the presence of a prostate neoplastic condition or pathology in the tested individual.

A detectable label can be useful in a method of the invention and refers to a molecule that renders a nucleic acid molecule of the invention detectable by an analytical method. An appropriate detectable label depends on the particular assay format; such labels are well known by those skilled in the art. For example, a detectable label selective for a nucleic acid molecule

can be a complementary nucleic acid molecule, such as a hybridization probe, that selectively hybridizes to the nucleic acid molecule. A hybridization probe can be labeled with a measurable moiety, such as a radioisotope, fluorochrome, chemiluminescent marker, biotin, or other moiety known in the art that is measurable by analytical methods. A detectable label also can be a nucleic acid molecule without a measurable moiety. For example, PCR or RT-PCR primers can be used without conjugation to selectively amplify all or a desired portion of the nucleic acid molecule. The amplified nucleic acid molecules can then be detected by methods known in the art.

The present invention also provide diagnostic methods that rely on a binding agent that selectively binds the specified ARP polypeptide. In particular, the present invention provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP7 binding agent that selectively binds an ARP7 polypeptide; determining a test expression level of ARP7 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP7 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced with a specimen that includes, for example, prostate tissue, or with a specimen which is blood, serum, urine or semen. If desired, a method of the invention for diagnosing or predicting susceptibility to a prostate neoplastic condition can be practiced with an ARP7 binding agent which is an antibody. In one embodiment, a method of the invention is practiced with

an ARP7 binding agent that selectively binds human ARP7 (SEQ ID NO: 2).

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP15 binding agent that selectively binds an ARP15 polypeptide; determining a test expression level of ARP15 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP15 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in such a method can include, for example, prostate tissue, or can be, for example, blood, serum, urine or semen. In one embodiment, the ARP15 binding agent that selectively binds the ARP15 polypeptide is an antibody. In another embodiment, a method of the invention is practiced with an ARP15 binding agent that selectively binds human ARP15 (SEQ ID NO: 4).

Also provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP16 binding agent that selectively binds an ARP16 polypeptide; determining a test expression level of ARP16 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP16 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful for diagnosing or predicting susceptibility to a prostate neoplastic

condition can include, for example, prostate tissue, or can be, for example, a specimen of blood, serum, urine or semen. In one embodiment, the ARP16 binding agent is an antibody. In a further embodiment, a method of the invention is practiced with an ARP16 binding agent that selectively binds human ARP16 (SEQ ID NO: 6). In another embodiment, a method of the invention is practiced with an ARP16 binding agent that selectively binds at least eight contiguous amino acids of residues 1-465 of SEQ ID NO: 6.

There is further provided herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP8 binding agent that selectively binds an ARP8 polypeptide; determining a test expression level of ARP8 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP8 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced, for example, with a specimen that includes prostate tissue, or with a specimen which is blood, serum, urine or semen. In one embodiment, the ARP8 binding agent is an antibody. In another embodiment, the ARP8 binding agent selectively binds at least eight contiguous amino acids of human ARP8 (SEQ ID NO: 8). In a further embodiment, the ARP8 binding agent selectively binds at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8. In yet a further embodiment, the ARP8 binding agent selectively binds residues 249-576 of SEQ ID NO: 8.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, in which a specimen from the individual is contacted with an ARP9 binding agent that selectively binds an ARP9 polypeptide; a test expression level of ARP9 polypeptide in the specimen is determined; and the test expression level is compared to a non-neoplastic control expression level of ARP9 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A method of the invention can be practiced with a specimen containing, for example, prostate tissue, or, for example, with a blood, serum, urine or semen specimen. If desired, a method of the invention can be practiced with an ARP9 binding agent which is an antibody. In one embodiment, a method of the invention is practiced with an ARP9 binding agent that selectively binds at least eight contiguous amino acids of human ARP9 (SEQ ID NO: 10).

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP13 binding agent that selectively binds an ARP13 polypeptide; determining a test expression level of ARP13 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP13 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A variety of specimens are useful in a method of the invention for diagnosing or predicting susceptibility to a prostate neoplastic condition, including, but not limited to, prostate tissue, blood,

serum, urine and semen. An ARP13 binding agent useful in a method of the invention can be, for example, an antibody. An ARP13 binding agent useful in the invention also can be an ARP13 binding agent that selectively binds at least eight contiguous amino acids of human ARP13 (SEQ ID NO: 12).

Further provided herein is a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP20 binding agent that selectively binds an ARP20 polypeptide; determining a test expression level of ARP20 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP20 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. In one embodiment, a method of the invention is practiced with a specimen of prostate tissue. In another embodiment, a method of the invention is practiced with a blood, serum, urine or semen specimen. In a further embodiment, a method of the invention is practiced with an ARP20 binding agent which is an antibody. In yet a further embodiment, a method of the invention is practiced with an ARP20 binding agent that selectively binds at least eight contiguous amino acids of human ARP20 (SEQ ID NO: 14).

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP24 binding agent that selectively binds an ARP24 polypeptide; determining a test expression level of ARP24 polypeptide in the specimen; and comparing the test expression level to a

non-neoplastic control expression level of ARP24 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. Samples useful in a method of the invention include prostate tissue, blood, urine and semen. In one embodiment, a method of the invention is practiced with an ARP24 nucleic acid molecule having a length of 15 to 35 nucleotides. In another embodiment, a method of the invention is practiced with an ARP24 binding agent that selectively binds at least eight contiguous amino acids of human ARP24 (SEQ ID NO: 16).

The invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP26 binding agent that selectively binds an ARP26 polypeptide; determining a test expression level of ARP26 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP26 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. In one embodiment, the ARP26 binding agent is an antibody. In another embodiment, the ARP26 binding agent selectively binds at least eight contiguous amino acids of human ARP26 (SEQ ID NO: 18).

The invention further provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP28 binding agent

the selectively binds an ARP28 polypeptide; determining a test expression level of ARP28 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP28 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. ARP28 binding agents useful in the methods of the invention include, but are not limited to, antibodies. In one embodiment, a method of the invention is practiced with an ARP28 binding agent that selectively binds at least eight contiguous amino acids of human ARP28 (SEQ ID NO: 20).

The invention also provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP30 binding agent that selectively binds an ARP30 polypeptide; determining a test expression level of ARP30 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP30 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. ARP30 binding agents useful in the methods of the invention include, but are not limited to, antibodies. Additional ARP30 binding agents useful in the invention include those that selectively bind at least eight contiguous amino acids of human ARP30 (SEQ ID NO: 22).

The invention also provides herein a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP33 binding agent that selectively binds an ARP33 polypeptide; determining a test expression level of ARP33 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP33 polypeptide, where an altered test expression level as compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. A specimen useful in the invention can include, for example, prostate tissue, or can be, for example, a blood, serum, urine or semen specimen. ARP33 binding agents useful in the methods of the invention encompass, without limitation, antibodies. In one embodiment, a method of the invention is practiced with an ARP33 binding agent that selectively binds human ARP33 (SEQ ID NO: 24). In another embodiment, a method of the invention is practiced with an ARP33 binding agent that selectively binds at least eight contiguous amino acids of residues 1-132 of SEQ ID NO: 24. In yet a further embodiment, a method of the invention is practiced with an ARP33 binding agent that selectively binds at least eight contiguous amino acids of residues 251-405 of SEQ ID NO: 24.

The present invention also provides a method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual by contacting a specimen from the individual with an ARP11 binding agent that selectively binds an ARP11 polypeptide; determining a test expression level of ARP11 polypeptide in the specimen; and comparing the test expression level to a non-neoplastic control expression level of ARP11 polypeptide, where an altered test expression level as

compared to the control expression level indicates the presence of a prostate neoplastic condition in the individual. The method can be practiced with, for example, a prostate tissue specimen, or with a specimen of blood, serum, urine or semen. In one embodiment, a method of the invention is practiced with an ARP11 binding agent which is an antibody that selectively binds at least eight contiguous amino acids of human ARP11 (SEQ ID NO: 34).

In a method of the invention, the specimen can contain, for example, a prostate cell or prostate tissue and, in one embodiment, is a fluid such as blood, serum, urine or semen. The control expression level can be determined, for example, using a normal prostate cell or an androgen-dependent cell line. In addition, a binding agent selective for a polypeptide of the invention can be, for example, an antibody, and, if desired, can further include a detectable label.

As used herein, the term "specimen" means any biological material including fluid, cell, tissue, organ or portion thereof, that contains or potentially contains an ARP polypeptide of the invention. The term specimen includes materials present in an individual as well as materials obtained or derived from the individual. For example, a specimen can be a histologic section obtained by biopsy, or cells that are placed in or adapted to tissue culture. A specimen further can be a subcellular fraction or extract, or a crude or substantially pure protein preparation. A specimen can be prepared by methods known in the art suitable for the particular format of the detection method.

In methods of the invention, the specimen can be, for example, a prostate cell or prostate tissue such

as a tissue biopsy. A specimen can also be a fluid sample, for example, blood, serum, urine or semen. A normal specimen can be, for example, a normal prostate cell or an androgen-dependent cell line.

These diagnostic methods of the invention rely on a binding agent. As described above, the term "binding agent" when used in reference to an ARP polypeptide, is intended to mean a compound, including a simple or complex organic molecule, a metal containing compound, carbohydrate, peptide, protein, peptidomimetic, glycoprotein, lipoprotein, lipid, nucleic acid molecule, antibody, or the like that selectively binds the specified ARP polypeptide, or fragment thereof. The binding agent can be labeled with a detectable moiety, if desired, or rendered detectable by specific binding to a detectable secondary binding agent. Exemplary binding agents are discussed hereinabove.

A prostate neoplastic condition is a benign or malignant prostate lesion of proliferating cells. Prostate neoplastic conditions include, for example, prostate interepithelial neoplasia (PIN) and prostate cancer. Prostate cancer is an uncontrolled proliferation of prostate cells which can invade and destroy adjacent tissues as well as metastasize. Primary prostate tumors can be classified into stages TX, T0, T1, T2, T3, and T4 and metastatic tumors can be classified into stages D1, D2 and D3. Similarly, there are classifications known by those skilled in the art for the progressive stages of precancerous lesions or PIN. The methods herein are applicable for the diagnosis or treatment of any or all stages of prostate neoplastic conditions.

The methods of the invention are also applicable to prostate pathologies other than neoplastic

conditions. Such other pathologies include, for example, benign prostatic hyperplasia (BPH) and prostatitis. BPH is one of the most common diseases in adult males. Histological evidence of BPH has been found in more than 40% of men in their fifties and almost 90% of men in their eighties. The disease results from the accumulation of non-malignant nodules arising in a small region around the proximal segment of the prostatic urethra which leads to an increase in prostate volume. If left untreated, BPH can result in acute and chronic retention of urine, renal failure secondary to obstructive uropathy, serious urinary tract infection and irreversible bladder decompensation. Prostatitis is an infection of the prostate. Other prostate pathologies known to those skilled in the art exist as well and are similarly applicable for diagnosis or treatment using the methods of the invention. Various neoplastic conditions of the prostate as well as prostate pathologies can be found described in, for example, Campbell's Urology, Seventh Edition, W.B. Saunders Company, Philadelphia (1998). Therefore, the methods of the invention are applicable to both prostate neoplastic conditions and prostate pathologies.

Therefore, the invention provides a method for both diagnosing and prognosing a prostate neoplastic condition including prostate cancer and prostate interepithelial neoplasia as well as other prostate pathologies such as BPH and prostatitis.

The invention provides a method of diagnosing or predicting prostate neoplastic conditions based on a finding of a positive correlation between a test expression level of an ARP polypeptide or nucleic acid in neoplastic cells of the prostate and the degree or extent of the neoplastic condition or pathology. The diagnostic

methods of the invention are applicable to numerous prostate neoplastic conditions and pathologies as described above. One consequence of progression into these neoplastic and pathological conditions can be altered expression of ARP polypeptide or nucleic acid in prostate tissue. The alteration in ARP polypeptide or nucleic acid expression in individuals suffering from a prostate neoplastic condition can be measured by comparing the amount of ARP polypeptide or nucleic acid to that found, for example, in normal prostate tissue samples or in normal blood or serum samples. A two-fold or more increase or decrease in a test expression level in a prostate cell sample relative to a non-neoplastic control expression sample obtained, for example, from normal prostate cells or from an androgen-dependent cell line is indicative of a prostate neoplastic condition or pathology. Similarly, an alteration in ARP polypeptide or nucleic acid expression leading to an increased or decreased secretion into the blood or other circulatory fluids of the individual compared to a non-neoplastic control blood or fluid samples also can be indicative of a prostate neoplastic condition or pathology. For example, an alteration in ARP polypeptide or nucleic acid expression can lead to a two-fold, five-fold, ten-fold, 100-fold, 200-fold or 1000-fold increased secretion into the blood or other circulatory fluids of the individual compared to a non-neoplastic control blood or fluid samples. As another example, an alteration in ARP polypeptide or nucleic acid expression can lead to a two-fold, five-fold, ten-fold, 100-fold, 200-fold or 1000-fold decreased secretion into the blood or other circulatory fluids of the individual compared to a non-neoplastic control blood or fluid samples.

As a diagnostic indicator, an ARP polypeptide or nucleic acid molecule can be used qualitatively to

positively identify a prostate neoplastic condition or pathology as described above. Alternatively, ARP polypeptide or nucleic acid molecule also can be used quantitatively to determine the degree or susceptibility of a prostate neoplastic condition or pathology. For example, successive increases or decreases in the expression levels of ARP polypeptide or nucleic acid can be used as a predictive indicator of the degree or severity of a prostate neoplastic condition or pathology. For example, increased expression can lead to a rise in accumulated levels and can be positively correlated with increased severity of a neoplastic condition of the prostate. A higher level of ARP polypeptide or nucleic acid expression can be correlated with a later stage of a prostate neoplastic condition or pathology. For example, increases in expression levels of two-fold or more compared to a normal sample can be indicative of at least prostate neoplasia. ARP polypeptide or nucleic acid molecule also can be used quantitatively to distinguish between pathologies and neoplastic conditions as well as to distinguish between the different types of neoplastic conditions.

Correlative alterations can be determined by comparison of ARP polypeptide or nucleic acid expression from the individual having, or suspected of having, a neoplastic condition of the prostate to expression levels of ARP polypeptide or nucleic acid from known specimens or samples determined to exhibit a prostate neoplastic condition. Alternatively, correlative alterations also can be determined by comparison of a test expression level of ARP polypeptide or nucleic acid expression to expression levels of other known markers of prostate cancer such as prostate specific antigen (PSA), glandular kallikrein 2 (hK2) and prostase/PRSS18. These other known markers can be used, for example, as an internal or

external standard for correlation of stage-specific expression with altered ARP polypeptide or nucleic acid expression and severity of the neoplastic or pathological condition. Conversely, a regression in the severity of a prostate neoplastic condition or pathology can be followed by a corresponding reversal in ARP polypeptide or nucleic acid expression levels and can similarly be assessed using the methods described herein.

Given the teachings and guidance provided herein, those skilled in the art will know or can determine the stage or severity of a prostate neoplastic condition or pathology based on a determination of ARP polypeptide or nucleic acid expression and correlation with a prostate neoplastic condition or pathology. A correlation can be determined using known procedures and marker comparisons as described herein. For a review of recognized values for such other marker in normal versus pathological tissues, see, for example, Campbell's Urology, Seventh Edition, W.B. Saunders Company, Philadelphia (1998).

The use of ARP polypeptide or nucleic acid expression levels in prostate cells, the circulatory system and urine as a diagnostic indicator of a prostate pathology allows for early diagnosis as a predictive indicator when no physiological or pathological symptoms are apparent. The methods are particularly applicable to any males over age 50, African-American males and males with familial history of prostate neoplastic conditions or pathologies. The diagnostic methods of the invention also are particularly applicable to individuals predicted to be at risk for prostate neoplastic conditions or pathologies by reliable prognostic indicators prior to onset of overt clinical symptoms. All that is necessary is to determine the ARP polypeptide or nucleic acid

prostate tissue or circulatory or bodily fluid expression levels to determine whether there is altered ARP polypeptide or nucleic acid levels in the individual suspected of having a prostate pathology compared to a control expression level such as the level observed in normal individuals. Those skilled in the art will know by using routine examinations and practices in the field of medicine those individuals who are applicable candidates for diagnosis by the methods of the invention.

For example, individuals suspected of having a prostate neoplastic condition or pathology can be identified by exhibiting presenting signs of prostate cancer which include, for example, a palpable nodule (> 50% of the cases), dysuria, cystitis and prostatitis, frequency, urinary retention, or decreased urine stream. Signs of advanced disease include pain, uremia, weight loss and systemic bleeding. Prognostic methods of this invention are applicable to individuals after diagnosis of a prostate neoplastic condition, for example, to monitor improvements or identify residual neoplastic prostate cells using, for example, imaging methods known in the art and which target ARP polypeptide or nucleic acid. Therefore, the invention also provides a method of predicting the onset of a prostate neoplastic condition or pathology by determining an altered test expression level of one of the ARP nucleic acid molecules or polypeptides of the invention.

The diagnostic methods of the invention are applicable for use with a variety of different types of samples or specimens isolated or obtained from an individual having, or suspected of having a prostate neoplastic condition or prostate pathology. For example, samples applicable for use in one or more diagnostic formats of the invention include tissue and cell samples.

A tissue or cell sample or specimen can be obtained, for example, by biopsy or surgery. As described below, and depending on the format of the method, the tissue can be used whole or subjected to various methods known in the art to disassociate the sample or specimen into smaller pieces, cell aggregates or individual cells. Additionally, when combined with amplification methods such as polymerase chain reaction (PCR), a single prostate cell can be a sample sufficient for use in diagnostic assays of the invention which employ hybridization detection methods. Similarly, when measuring ARP polypeptide or activity levels, amplification of the signal with enzymatic coupling or photometric enhancement can be employed using only a few or a small number of cells.

Whole tissue obtained from a prostate biopsy or surgery is one example of a prostate cell sample or specimen. Whole tissue prostate cell samples or specimens can be assayed employing any of the formats described below. For example, the prostate tissue sample can be mounted and hybridized *in situ* with ARP nucleic acid probes. Similar histological formats employing protein detection methods and *in situ* activity assays also can be used to detect an ARP polypeptide in whole tissue prostate cell specimens. Protein detection methods include, for example, staining with an ARP specific antibody and activity assays. Such histological methods as well as others well known to those skilled in the art are applicable for use in the diagnostic methods of the invention using whole tissue as the source of a prostate cell specimen. Methods for preparing and mounting the samples and specimens are similarly well known in the art.

Individual prostate cells and cell aggregates from an individual having, or suspected of having a prostate neoplastic condition or pathology also are prostate cell samples which can be analyzed for an altered test expression level in a method of the invention. The cells can be grown in culture and analyzed *in situ* using procedures such as those described above. Whole cell samples expressing cell surface markers associated with ARP polypeptide or nucleic acid expression can be rapidly tested using fluorescent or magnetic activated cell sorting (FACS or MACS) with labeled binding agents selective for the surface marker or using binding agents selective for epithelial or prostate cell populations, for example, and then determining a test expression level of a specified ARP polypeptide or nucleic acid within this population. The test expression level can be determined using, for example, binding agents selective for polypeptides of the invention or by hybridization to a specific nucleic acid molecule of the invention. Other methods for measuring the expression level of ARP polypeptide or nucleic acid in whole cell samples are known in the art and are similarly applicable in any of the diagnostic formats described below.

The tissue or whole cell prostate cell sample or specimen obtained from an individual also can be analyzed for increased ARP polypeptide or nucleic acid expression by lysing the cell and measuring a test expression levels of ARP polypeptide or nucleic acid in the lysate, a fractionated portion thereof or a purified component thereof using any of diagnostic formats described herein. For example, if a hybridization format is used, ARP RNA can be amplified directly from the lysate using PCR, or other amplification procedures well known in the art such as RT-PCR, 5' or 3' RACE to

directly measure the expression levels of ARP nucleic acid molecules. RNA also can be isolated and probed directly such as by solution hybridization or indirectly by hybridization to immobilized RNA. Similarly, when determining a test expression level of ARP using polypeptide detection formats, lysates can be assayed directly, or they can be further fractionated to enrich for ARP polypeptide and its corresponding activity. Numerous other methods applicable for use with whole prostate cell samples are well known to those skilled in the art and can accordingly be used in the methods of the invention.

The prostate tissue or cell sample or specimen can be obtained directly from the individual or, alternatively, it can be obtained from other sources for testing. Similarly, a cell sample can be tested when it is freshly isolated or it can be tested following short or prolonged periods of cryopreservation without substantial loss in accuracy or sensitivity. If the sample is to be tested following an indeterminate period of time, it can be obtained and then cryopreserved, or stored at 4°C for short periods of time, for example. An advantage of the diagnostic methods of the invention is that they do not require histological analysis of the sample. As such, the sample can be initially disaggregated, lysed, fractionated or purified and the active component stored for later diagnosis.

The diagnostic methods of the invention are applicable for use with a variety of different types of samples and specimens other than prostate cell samples. For example, an ARP polypeptide or fragment thereof that is released into the extracellular space, including circulatory fluids as well as other bodily fluids, can be detected in a method of the invention. In such a case,

the diagnostic methods of the invention are practiced with fluid samples collected from an individual having, or suspected of having a neoplastic condition of the prostate or a prostate pathology.

Fluid samples and specimens, which can be measured for ARP polypeptide or nucleic acid expression levels, include, for example, blood, serum, lymph, urine and semen. Other bodily fluids are known to those skilled in the art and are similarly applicable for use as a sample or specimen in the diagnostic methods of the invention. One advantage of analyzing fluid samples or specimens is that they are readily obtainable, in sufficient quantity, without invasive procedures as required by biopsy and surgery. Analysis of fluid samples or specimens such as blood, serum and urine will generally be in the diagnostic formats described herein which measure ARP polypeptide levels or activity. As the ARP related polypeptide is circulating in a soluble form, the methods will be similar to those which measure expression levels from cell lysates, fractionated portions thereof or purified components.

Prostate neoplastic conditions and prostate pathologies can be diagnosed, predicted or prognosed by measuring a test expression level of ARP polypeptide or nucleic acid in a prostate cell sample, circulating fluid or other bodily fluid obtained from the individual. As described herein, a test or control expression level can be measured by a variety of methods known in the art. For example, a test expression level of a specified ARP can be determined by measuring the amount of ARP RNA or polypeptide in a sample or specimen from the individual. Alternatively, a test expression level of ARP can be determined by measuring the amount of an ARP activity in

a specimen, the amount of activity being indicative of the specified ARP polypeptide expression level.

One skilled in the art can readily determine an appropriate assay system given the teachings and guidance provided herein and choose a method based on measuring ARP RNA, polypeptide or activity. Considerations such as the sample or specimen type, availability and amount will also influence selection of a particular diagnostic format. For example, if the sample or specimen is a prostate cell sample and there is only a small amount available, then diagnostic formats which measure the amount of ARP RNA by, for example, PCR amplification, or which measure ARP-related cell surface polypeptide by, for example, FACS analysis can be appropriate choices for determining a test expression level. Alternatively, if the specimen is a blood sample and the user is analysing numerous different samples simultaneous, such as in a clinical setting, then a multisample format, such as an Enzyme Linked Immunoabsorbant Assay (ELISA), which measures the amount of an ARP polypeptide can be an appropriate choice for determining a test expression level of a specified ARP. Additionally, ARP nucleic acid molecules released into bodily fluids from the neoplastic or pathological prostate cells can also be analyzed by, for example, PCR or RT-PCR. Those skilled in the art will know, or can determine which format is amenable for a particular application and which methods or modifications known within the art are compatible with a particular type of format.

Hybridization methods are applicable for measuring the amount of ARP RNA as an indicator of ARP expression levels. There are numerous methods well known in the art for detecting nucleic acid molecules by specific or selective hybridization with a complementary

nucleic acid molecule. Such methods include both solution hybridization procedures and solid-phase hybridization procedures where the probe or sample is immobilized to a solid support. Descriptions for such methods can be found in, for example, Sambrook et al., *supra*, and in Ausubel et al., *supra*. Specific examples of such methods include PCR and other amplification methods such as RT-PCR, 5' or 3' RACE, RNase protection, RNA blot, dot blot or other membrane-based technologies, dip stick, pin, ELISA or two-dimensional arrays immobilized onto chips as a solid support. These methods can be performed using either qualitative or quantitative measurements, all of which are well known to those skilled in the art.

PCR or RT-PCR can be used with isolated RNA or crude cell lysate preparations. As described previously, PCR is advantageous when there is limiting amounts of starting material. A further description of PCR methods can be found in, for example, Dieffenbach, C.W., and Dveksler, G.S., PCR Primer: A Laboratory Manual, Cold Spring Harbor Press, Plainview, New York (1995). Multisample formats such as an ELISA or two-dimensional array offer the advantage of analyzing numerous, different samples in a single assay. Solid-phase dip stick-based methods offer the advantage of being able to rapidly analyze a patient's fluid sample and obtain an immediate result.

Nucleic acid molecules useful for measuring a test expression level of a specified ARP RNA are disclosed herein above. Briefly, for detection by hybridization, an ARP nucleic acid molecule having a detectable label is added to a prostate cell sample or a fluid sample obtained from the individual having, or suspected of having a prostate neoplastic condition or

pathology under conditions which allow annealing of the molecule to an ARP RNA. Methods for detecting ARP RNA in a sample can include the use of, for example, RT-PCR. Conditions are well known in the art for both solution and solid phase hybridization procedures. Moreover, optimization of hybridization conditions can be performed, if desired, by hybridization of an aliquot of the sample at different temperatures, durations and in different buffer conditions. Such procedures are routine and well known to those skilled in the art. Following annealing, the sample is washed and the signal is measured and compared with a suitable control or standard value. The magnitude of the hybridization signal is directly proportional to the expression levels of ARP RNA.

The diagnostic procedures described herein can additionally be used in conjunction with other prostate markers, such as prostate specific antigen, human glandular kallikrein 2 (hk2) and prostase/PRSS18 for simultaneous or independent corroboration of a sample. Additionally, ARP polypeptide or nucleic acid expression can be used, for example, in combination with other markers to further distinguish normal basal cells, secretory cells and neoplastic cells of the prostate. Moreover, ARP polypeptide or nucleic acid expression can be used in conjunction with smooth muscle cell markers to distinguish between pathological conditions such as benign prostate hypertrophy (BPH) and neoplasia. Those skilled in the art will know which markers are applicable for use in conjunction with ARP polypeptide or nucleic acid to delineate more specific diagnostic information such as that described above.

The invention also provides diagnostic methods based on determining whether there is an altered test

expression level of an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide using a binding agent that selectively binds at least eight contiguous amino acids of the recited polypeptide. Essentially all modes of affinity binding assays are applicable for use in determining a test expression level of an ARP polypeptide in a method of the invention. Such methods are rapid, efficient and sensitive. Moreover, affinity binding methods are simple and can be modified to be performed under a variety of clinical settings and conditions to suit a variety of particular needs. Affinity binding assays which are known and can be used in the methods of the invention include both soluble and solid phase formats. A specific example of a soluble phase affinity binding assay is immunoprecipitation using an ARP selective antibody or other binding agent. Solid phase formats are advantageous in that they are rapid and can be performed easily and simultaneously on multiple different samples without losing sensitivity or accuracy. Moreover, solid phase affinity binding assays are further amenable to high throughput and ultra high throughput screening and automation.

Specific examples of solid phase affinity binding assays include immunoaffinity binding assays such as an ELISA and radioimmune assay (RIA). Other solid phase affinity binding assays are known to those skilled in the art and are applicable to the methods of the invention. Although affinity binding assays are generally formatted for use with an antibody binding molecule that is selective for the analyte or ligand of interest, essentially any binding agent can be alternatively substituted for the selectively binding antibody. Such binding agents include, for example, macromolecules such as polypeptides, peptides, nucleic acid molecules, lipids and sugars as well as small

molecule compounds. Methods are known in the art for identifying such molecules which bind selectively to a particular analyte or ligand and include, for example, surface display libraries and combinatorial libraries. Thus, for a molecule other than an antibody to be used in an affinity binding assay, all that is necessary is for the binding agent to exhibit selective binding activity for a polypeptide of the invention.

Various modes of affinity binding formats are similarly known which can be used in the diagnostic methods of the invention. For the purpose of illustration, particular embodiments of such affinity binding assays will be described further in reference to immunoaffinity binding assays. The various modes of affinity binding assays, such as immunoaffinity binding assays, include, for example, solid phase ELISA and RIA as well as modifications thereof. Such modifications thereof include, for example, capture assays and sandwich assays as well as the use of either mode in combination with a competition assay format. The choice of which mode or format of immunoaffinity binding assay to use will depend on the intent of the user. Such methods can be found described in common laboratory manuals such as Harlow and Lane, Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York (1999).

As with the hybridization methods described previously, the diagnostic formats employing affinity binding can be used in conjunction with a variety of detection labels and systems known in the art to quantitate amounts of a polypeptide of the invention in the analyzed sample. Detection systems include the detection of bound polypeptide on the invention by both direct and indirect means. Direct detection methods include labeling of the ARP-selective antibody or binding

agent. Indirect detection systems include, for example, the use of labeled secondary antibodies and binding agents.

Secondary antibodies, labels and detection systems are well known in the art and can be obtained commercially or by techniques well known in the art. The detectable labels and systems employed with the ARP-selective binding agent should not impair binding of the agent to the corresponding ARP polypeptide. Moreover, multiple antibody and label systems can be employed for detecting the bound ARP-selective antibody to enhance the sensitivity of the binding assay if desired.

As with the hybridization formats described previously, detectable labels can be essentially any label that can be quantitated or measured by analytical methods. Such labels include, for example, enzymes, radioisotopes, fluorochromes as well as chemi- and bioluminescent compounds. Specific examples of enzyme labels include horseradish peroxidase (HRP), alkaline phosphatase (AP), β-galactosidase, urease and luciferase.

A horseradish-peroxidase detection system can be used, for example, with the chromogenic substrate tetramethylbenzidine (TMB), which yields a soluble product in the presence of hydrogen peroxide that is detectable by measuring absorbance at 450 nm. An alkaline phosphatase detection system can be used with the chromogenic substrate *p*-nitrophenyl phosphate, for example, which yields a soluble product readily detectable by measuring absorbance at 405 nm. Similarly, a β-galactosidase detection system can be used with the chromogenic substrate *o*-nitrophenyl-β-D-galactopyranoside (ONPG), which yields a soluble product detectable by

measuring absorbance at 410 nm, or a urease detection system can be used with a substrate such as urea-bromocresol purple (Sigma Immunochemicals, St. Louis, MO). Luciferin is the substrate compound for luciferase which emits light following ATP-dependent oxidation.

Fluorochrome detection labels are rendered detectable through the emission of light of ultraviolet or visible wavelength after excitation by light or another energy source. DAPI, fluorescein, Hoechst 33258, R-phycocyanin, B-phycoerythrin, R-phycoerythrin, rhodamine, Texas red and lissamine are specific examples of fluorochrome detection labels that can be utilized in the affinity binding formats of the invention. A particularly useful fluorochrome is fluorescein or rhodamine.

Chemiluminescent as well as bioluminescent detection labels are convenient for sensitive, non-radioactive detection of an ARP polypeptide and can be obtained commercially from various sources such as Amersham Lifesciences, Inc. (Arlington Heights, IL).

Alternatively, radioisotopes can be used as detectable labels in the methods of the invention. Iodine-125 is a specific example of a radioisotope useful as a detectable label.

Signals from detectable labels can be analyzed, for example, using a spectrophotometer to detect color from a chromogenic substrate; a fluorometer to detect fluorescence in the presence of light of a certain wavelength; or a radiation counter to detect radiation, such as a gamma counter for detection of iodine-125. For detection of an enzyme-linked secondary antibody, for

example, a quantitative analysis of the amount of bound agent can be made using a spectrophotometer such as an EMAX Microplate Reader (Molecular Devices, Menlo Park, CA) in accordance with the manufacturer's instructions. If desired, the assays of the invention can be automated or performed robotically, and the signal from multiple samples can be detected simultaneously.

The diagnostic formats of the present invention can be forward, reverse or simultaneous as described in U.S. Patent No. 4,376,110 and No. 4,778,751. Separation steps for the various assay formats described herein, including the removal of unbound secondary antibody, can be performed by methods known in the art (Harlow and Lane, *supra*). For example, washing with a suitable buffer can be followed by filtration, aspiration, vacuum or magnetic separation as well as by centrifugation.

A binding agent selective for an ARP polypeptide also can be utilized in imaging methods that are targeted at ARP expressing prostate cells. These imaging techniques have utility in identification of residual neoplastic cells at the primary site following standard treatments including, for example, radical prostatectomy, radiation or hormone therapy. In addition, imaging techniques that detect neoplastic prostate cells have utility in detecting secondary sites of metastasis. A binding agent that selectively binds an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide can be radiolabeled with, for example, ^{111}indium and infused intravenously as described by Kahn et al., Journal of Urology 152:1952-1955 (1994). The binding agent selective for an ARP polypeptide can be, for example, a monoclonal antibody selective for an ARP polypeptide. Imaging can be accomplished by, for

example, radioimmunoscintigraphy as described by Kahn et al., *supra*.

In one embodiment, the invention provides a method of diagnosing or predicting the susceptibility of a prostate neoplastic condition in an individual suspected of having a neoplastic condition of the prostate, where a test expression level of an ARP polypeptide is determined by measuring the amount of ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide activity. The method is practiced by contacting a specimen from the individual with an agent that functions to measure an activity associated with an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide of the invention.

As with the hybridization and affinity binding formats described above, activity assays similarly can be performed using essentially identical methods and modes of analysis. Therefore, solution and solid phase modes, including multisample ELISA, RIA and two-dimensional array procedures are applicable for use in measuring an activity associated with an ARP polypeptide. The activity can be measured by, for example, incubating an agent that functions to measure an activity associated with an ARP polypeptide with the sample and determining the amount of product formed that corresponds to ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide activity. The amount of product formed will directly correlate with the ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide activity in the specimen and therefore, with the expression levels of the corresponding polypeptide of the invention in the specimen.

The invention further provides a method of identifying a compound that inhibits ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide activity. The method consists of contacting a specimen containing an ARP polypeptide and an agent that functions to measure an activity associated with an ARP polypeptide with a test compound under conditions that allow formation of a product that corresponds to an ARP polypeptide activity and measuring the amount of product formed, where a decrease in the amount of product formed in the presence of the test compound compared to the absence of the test compound indicates that the compound has ARP polypeptide inhibitory activity. Similarly, compounds that increase the activity of an ARP polypeptide also can be identified. A test compound added to a specimen containing an ARP polypeptide and an agent that functions to measure an activity associated with an ARP polypeptide which increases the amount of product formed compared to the absence of the test compound indicates that the compound increases the corresponding ARP polypeptide activity. Therefore, the invention provides a method of identifying compounds that modulate the activity of an ARP polypeptide. The ARP polypeptide containing specimen used for such a method can be serum, prostate tissue, a prostate cell population or a recombinant cell population expressing an ARP polypeptide.

Those compounds having inhibitory activity are considered as potential ARP polypeptide antagonists and further as potential therapeutic agents for treatment of neoplastic conditions of the prostate. Similarly, those compounds which increase an ARP polypeptide activity are considered as potential ARP polypeptide agonists and further as potential therapeutic agents for the treatment of neoplastic conditions of the prostate. Each of these

classes of compounds is encompassed by the term ARP regulatory agent as defined herein.

Within the biological arts, the term "about" when used in reference to a particular activity or measurement is intended to refer to the referenced activity or measurement as being within a range of values encompassing the referenced value and within accepted standards of a credible assay within the art, or within accepted statistical variance of a credible assay within the art.

A reaction system for identifying a compound that inhibits or enhances an ARP polypeptide activity can be performed using essentially any source of ARP polypeptide activity. Such sources include, for example, a prostate cell sample, lysate or fractionated portion thereof; a bodily fluid such as blood, serum or urine from an individual with a prostate neoplastic condition; a recombinant cell or soluble recombinant source, and an *in vitro* translated source. The ARP polypeptide source is combined with an agent that functions to measure an activity associated with an ARP polypeptide as described above and incubated in the presence or absence of a test inhibitory compound. The amount of product that corresponds to an ARP polypeptide activity that is formed in the presence of the test compound is compared with that in the absence of the test compound. Those test compounds which inhibit product formation are considered to be ARP polypeptide inhibitors. For example, a test compound can inhibit product formation by at least 50%, 80%, 90%, 95%, 99%, 99.5% or 99.9%. Similarly, those compounds which increase product formation are considered to be ARP polypeptide enhancers or activators. For example, a test compound can increase product formation by at least two-fold, five-fold, ten-fold, 100-fold, 200-

fold or 1000-fold. ARP polypeptide inhibitors and activators can then be subjected to further *in vitro* or *in vivo* testing to confirm that they inhibit an ARP polypeptide activity in cellular and animal models.

Suitable test compounds for the inhibition or enhancement assays can be any substance, molecule, compound, mixture of molecules or compounds, or any other composition which is suspected of being capable of inhibiting an ARP polypeptide activity *in vivo* or *in vitro*. The test compounds can be macromolecules, such as biological polymers, including proteins, polysaccharides and nucleic acid molecules. Sources of test compounds which can be screened for ARP polypeptide inhibitory activity include, for example, libraries of peptides, polypeptides, DNA, RNA and small organic compounds. The test compounds can be selected randomly and tested by the screening methods of the present invention. Test compounds are administered to the reaction system at a concentration in the range from about 1 pM to 1 mM.

Methods for producing pluralities of compounds to use in screening for compounds that modulate the activity of an ARP polypeptide, including chemical or biological molecules that are inhibitors or enhancers of an ARP activity such as simple or complex organic molecules, metal-containing compounds, carbohydrates, peptides, proteins, peptidomimetics, glycoproteins, lipoproteins, nucleic acid molecules, antibodies, and the like, are well known in the art and are described, for example, in Huse, U.S. Patent No. 5,264,563; Francis et al., Curr. Opin. Chem. Biol. 2:422-428 (1998); Tietze et al., Curr. Biol., 2:363-371 (1998); Sofia, Mol. Divers. 3:75-94 (1998); Eichler et al., Med. Res. Rev. 15:481-496 (1995); and the like. Libraries containing large numbers of natural and synthetic compounds also can be obtained

from commercial sources. Combinatorial libraries of molecules can be prepared using well known combinatorial chemistry methods (Gordon et al., J. Med. Chem. 37: 1233-1251 (1994); Gordon et al., J. Med. Chem. 37: 1385-1401 (1994); Gordon et al., Acc. Chem. Res. 29:144-154 (1996); Wilson and Czarnik, eds., Combinatorial Chemistry: Synthesis and Application, John Wiley & Sons, New York (1997)).

Therefore, the invention provides a method of identifying a compound that inhibits or enhances an ARP polypeptide activity where the sample further consists of a prostate cell lysate, a recombinant cell lysate expressing an ARP polypeptide, an *in vitro* translation lysate containing an ARP mRNA, a fraction of a prostate cell lysate, a fraction of a recombinant cell lysate expressing an ARP polypeptide, a fractionated sample of an *in vitro* translation lysate containing an ARP mRNA or an isolated ARP polypeptide. The method can be performed in single or multiple sample format.

In another embodiment, polypeptides of the invention can be used as vaccines to prophylactically treat individuals for the occurrence of a prostate neoplastic condition or pathology. Such vaccines can be used to induce B or T cell immune responses or both aspects of the individuals endogenous immune mechanisms. The mode of administration and formulations to induce either or both of these immune responses are well known to those skilled in the art. For example, polypeptides can be administered in many possible formulations, including pharmaceutically acceptable mediums. They can be administered alone or, for example, in the case of a peptide, the peptide can be conjugated to a carrier, such as KLH, in order to increase its immunogenicity. The vaccine can include or be administered in conjunction

with an adjuvant, various of which are known to those skilled in the art. After initial immunization with the vaccine, further boosters can be provided if desired. Therefore, the vaccines are administered by conventional methods in dosages which are sufficient to elicit an immunological response, which can be easily determined by those skilled in the art. Alternatively, the vaccines can contain anti-idiotypic antibodies which are internal images of polypeptides of the invention. Methods of making, selecting and administering such anti-idiotype vaccines are well known in the art. See, for example, Eichmann, et al., CRC Critical Reviews in Immunology 7:193-227 (1987). In addition, the vaccines can contain an ARP nucleic acid molecule. Methods for using nucleic acid molecules such as DNA as vaccines are well known to those skilled in the art (see, for example, Donnelly et al. (Ann. Rev. Immunol. 15:617-648 (1997)); Felgner et al. (U.S. Patent No. 5,580,859, issued December 3, 1996); Felgner (U.S. Patent No.5,703,055, issued December 30, 1997); and Carson et al. (U.S. Patent No. 5,679,647, issued October 21, 1997)).

The invention additionally provides a method of treating or reducing the severity of a prostate neoplastic condition.

Also provided by the invention is a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to the individual an ARP7, ARP15, ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP26, ARP28, ARP30, ARP33 or ARP11 regulatory agent.

The invention further provides a method for treating or reducing the severity of a prostate neoplastic condition in an individual by administering to

the individual an ARP6, ARP10, ARP12, ARP18, ARP19, ARP21, ARP22 or ARP29 regulatory agent.

A method of the invention can be practiced by administering to an individual having a prostate neoplastic condition or other prostatic pathology an ARP7, ARP15, ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP26, ARP28, ARP30, ARP33 or ARP11 regulatory agent. A "regulatory agent" means an agent that inhibits or enhances a biological activity of the specified ARP polypeptide. Such an ARP regulatory agent can effect the amount of ARP polypeptide produced or can inhibit or enhance activity without effecting the amount of polypeptide. Such an ARP regulatory agent can be, for example, a dominant negative form of ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 polypeptide; an ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP30, ARP33 or ARP11 selective binding agent, or an ARP7, ARP15, ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP26, ARP28, ARP30, ARP33 or ARP11 antisense molecule. One skilled in the art understands that such an ARP7, ARP15, ARP16, ARP8, ARP9, ARP13, ARP20, ARP24, ARP26, ARP28, ARP30, ARP33 or ARP11 regulatory agent can be an agent that selectively regulates a biological activity of the specified ARP polypeptide or, alternatively, can be a non-selective agent that, in addition to regulating a biological activity of the specified polypeptide, also regulates the activity of one or more polypeptides.

A ARP regulatory agent can cause a two-fold, five-fold, ten-fold, 20-fold, 100-fold or more reduction in the amount or activity of an ARP polypeptide. As another example, a regulatory agent can cause a two-fold, five-fold, ten-fold, 20-fold, 100-fold or more increase in the amount or activity of an ARP polypeptide or nucleic acid. ARP regulatory agents include ARP nucleic

acid molecules, for example, antisense nucleic acid molecules; other nucleic acid molecules such as ribozymes; binding agents including antibodies, and compounds identified by the methods described herein. Such regulatory agents can be useful as therapeutics for treating or reducing the severity of an individual with a prostate neoplastic condition or for treating another pathology of the prostate.

One type of ARP regulatory agent is an inhibitor, means an agent effecting a decrease in the extent, amount or rate of ARP polypeptide expression or activity. An example of an ARP inhibitor is an ARP antisense nucleic acid molecule or a transcriptional inhibitor that binds to an ARP 5' promoter/regulatory region.

The term inhibitory amount means the amount of an inhibitor necessary to effect a reduction in the extent, amount or rate of ARP polypeptide. For example, an inhibitory amount of inhibitor can cause a two-fold, five-fold, ten-fold, 20-fold, 100-fold or more reduction in the amount or activity of an ARP polypeptide of the invention.

Such inhibitors can be produced using methods which are generally known in the art, and include the use of a purified ARP polypeptide to produce antibodies or to screen libraries of compounds, as described previously, for those which specifically bind a corresponding ARP polypeptide. For example, in one aspect, antibodies which are selective for an ARP polypeptide of the invention can be used directly as an antagonist, or indirectly as a targeting or delivery mechanism for bringing a cytotoxic or cytostatic agent to neoplastic prostate cells. Such agents can be, for example,

radioisotopes. The antibodies can be generated using methods that are well known in the art and include, for example, polyclonal, monoclonal, chimeric, humanized single chain, Fab fragments, and fragments produced by a Fab expression library.

In another embodiment of the invention, ARP polynucleotides, or any fragment thereof, or antisense molecules, can be used as an ARP regulatory agent in a method of the invention. In one aspect, antisense molecules to an ARP encoding nucleic acid molecules can be used to block the transcription or translation of the corresponding mRNA. Specifically, cells can be transformed with sequences complementary to a nucleic acid molecule of the invention. Such methods are well known in the art, and sense or antisense oligonucleotides or larger fragments, can be designed from various locations along the coding or control regions of sequences encoding ARP polypeptides or nucleic acids. Thus, antisense molecules may be used to modulate an ARP activity, or to achieve regulation of an ARP gene function.

Expression vectors derived from retroviruses, adenovirus, adeno-associated virus (AAV), herpes or vaccinia viruses, or from various bacterial plasmids can be used for delivery of antisense nucleotide sequences to the prostate cell population. The viral vector selected should be able to infect the tumor cells and be safe to the host and cause minimal cell transformation. Retroviral vectors and adenoviruses offer an efficient, useful, and presently the best-characterized means of introducing and expressing foreign genes efficiently in mammalian cells. These vectors are well known in the art and have very broad host and cell type ranges, express genes stably and efficiently. Methods which are well

known to those skilled in the art can be used to construct such recombinant vectors and are described in Sambrook et al., supra. Even in the absence of integration into the DNA, such vectors can continue to transcribe RNA molecules until they are disabled by endogenous nucleases. Transient expression can last for a month or more with a non-replicating vector and even longer if appropriate replication elements are part of the vector system.

Ribozymes, which are enzymatic RNA molecules, can also be used to catalyze the specific cleavage of an ARP mRNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target ARP RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within any potential RNA target are identified by scanning an ARP RNA for ribozyme cleavage sites which include the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides corresponding to the region of the target gene containing the cleavage site can be evaluated for secondary structural features which can render the oligonucleotide inoperable. The suitability of candidate targets can also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays. Antisense molecules and ribozymes of the invention can be prepared by any method known in the art for the synthesis of nucleic acid molecules.

In another embodiment, an ARP promoter and regulatory region can be used for constructing vectors for prostate cancer gene therapy. The promoter and regulatory region can be fused to a therapeutic gene for prostate specific expression. This method can include

the addition of one or more enhancer elements which amplify expression of the heterologous therapeutic gene without compromising tissue specificity. Methods for identifying a gene promoter and regulatory region are well known to those skilled in the art, for example, by selecting an appropriate primer from the 5' end of the coding sequence and isolating the promoter and regulatory region from genomic DNA.

Examples of therapeutic genes that are candidates for prostate gene therapy utilizing an ARP promoter include suicide genes. The expression of suicide genes produces a protein or agent that directly or indirectly inhibits neoplastic prostate cell growth or promotes neoplastic prostate cell death. Suicide genes include genes encoding enzymes, oncogenes, tumor suppressor genes, genes encoding toxins, genes encoding cytokines, or a gene encoding oncostatin. The therapeutic gene can be expressed using the vectors described previously for antisense expression.

In accordance with another embodiment of the present invention, there are provided diagnostic systems, for example, in kit form. Such a diagnostic system contains at least one nucleic acid molecule or antibody of the invention in a suitable packaging material. The diagnostic kits containing nucleic acid molecules are derived from ARP nucleic acid molecules described herein. A diagnostic system of the invention can be useful for assaying for the presence or absence of an ARP nucleic acid molecule in either genomic DNA or mRNA.

A suitable diagnostic system includes at least one ARP nucleic acid molecule or antibody, as a separately packaged chemical reagent(s) in an amount sufficient for at least one assay. For a diagnostic kit

containing a nucleic acid molecule of the invention, the kit will generally contain two or more nucleic acid molecules. When the diagnostic kit is to be used in PCR, the kit can further contain at least two oligonucleotides that can serve as primers for PCR. Those of skill in the art can readily incorporate nucleic acid molecules antibodies of the invention into kit form in combination with appropriate buffers and solutions for the practice of the invention methods as described herein. A kit containing an ARP polypeptide-specific antibody can contain a reaction cocktail that provides the proper conditions for performing an assay, for example, an ELISA or other immunoassay, for determining the level of expression of a corresponding ARP polypeptide in a specimen, and can contain control samples that contain known amounts of a corresponding ARP polypeptide and, if desired, a second antibody selective for the corresponding anti-ARP antibody.

The contents of the kit of the invention, for example, ARP nucleic acid molecules or antibodies, are contained in packaging material, which can provide a sterile, contaminant-free environment. In addition, the packaging material contains instructions indicating how the materials within the kit can be employed both to detect the presence or absence of a particular nucleic acid sequence or polypeptide of the invention or to diagnose the presence of, or a predisposition for a condition associated with the presence or absence of a nucleic acid sequence or polypeptide of the invention such as prostate cancer. The instructions for use typically include a tangible expression describing the reagent concentration or at least one assay method parameter, such as the relative amounts of reagent and sample to be admixed, maintenance time periods for

reagent concentration or at least one assay method parameter, such as the relative amounts of reagent and sample to be admixed, maintenance time periods for reagent/sample admixtures, temperature, buffer conditions, and the like.

All journal article, reference, and patent citations provided above, in parentheses or otherwise, whether previously stated or not, are incorporated herein by reference.

It is understood that modifications which do not substantially affect the activity of the various embodiments of this invention are also included within the definition of the invention provided herein. Accordingly, the following examples are intended to illustrate but not limit the present invention.

EXAMPLE I

Isolation of ARP cDNAs

This example describes the isolation of several androgen-regulated sequences.

The ARP7 cDNA was identified as an androgen upregulated sequence as described below. The ARP7 (SEQ ID NO: 1) contains 5470 nucleotides. Nucleotides 474 to 4967 encode a polypeptide of 1498 amino acids (SEQ ID NO: 2). As shown in Figure 1, ARP7 is dramatically up-regulated by androgen in starved LNCaP cells. As further shown in Figure 2, ARP7 is most highly expressed in the prostate with little or no detectable expression in other tissues.

The human ARP15 cDNA (SEQ ID NO: 3), which contains 3070 nucleotides, has an open reading frame from

transmembrane domains (see Table 1). As shown in Figure 3, ARP15 is expressed in prostate tissue and also expressed in testis and ovary.

The human ARP16 cDNA, shown herein as SEQ ID NO: 5, is a sequence of 2161 nucleotides with an open reading frame from nucleotide 138 to 1601. Furthermore, the human ARP16 is a polypeptide of 488 amino acids (SEQ ID NO: 4) with at least eight predicted transmembrane domains. As shown in Figure 1, ARP16 mRNA is dramatically up-regulated by androgen in starved LNCaP cells.

ARP8 also was identified as a human sequence up-regulated by androgen in prostate cells. The human ARP8 cDNA (SEQ ID NO: 7) contains 2096 nucleotides with an open reading frame from nucleotides 1 to 1728; the encoded human ARP8 polypeptide (SEQ ID NO: 8) has 576 amino acids. The nucleic acid sequence of another human androgen-regulated cDNA expressed in prostate, ARP9 (SEQ ID NO: 9), was identified as described below. The ARP9 nucleic acid sequence disclosed herein has 2568 nucleotides with an open reading frame from nucleotide 559 to 2232. The encoded human ARP9 polypeptide (SEQ ID NO: 10) has 558 residues and is predicted to include at least four transmembrane domains. The ARP13 cDNA also increased in response to androgen in the LNCaP cell line. The ARP13 nucleotide sequence (SEQ ID NO: 11) has 2920 nucleotides with an open reading frame from nucleotide 141 to 1022. The human ARP13 polypeptide has the 294 amino acid sequence shown herein as SEQ ID NO: 12 and is predicted to include at least one transmembrane domain. The ARP20 nucleotide sequence shown herein as SEQ ID NO: 13 also was identified as positively regulated in response to androgen in LNCaP cells. The human ARP20 nucleotide sequence has 1095 nucleotides with an open

reading frame from nucleotides 113 to 661; the human ARP20 polypeptide is shown herein as SEQ ID NO: 14.

ARP24, ARP26, ARP28, ARP30, ARP33 and ARP11 also were identified as androgen upregulated cDNAs expressed in the LnCaP prostate cell line. The ARP24 cDNA sequence shown herein as SEQ ID NO: 15 contains 3007 nucleotides with an open reading frame from nucleotides 38 to 1378; the encoded human ARP24 polypeptide has a 447 amino acid sequence (SEQ ID NO: 16) that is predicted to encode at least four transmembrane domains. The ARP26 cDNA sequence shown herein as SEQ ID NO: 17 was identified as a sequence of 3937 nucleotides with an open reading frame from nucleotides 240 to 1013. The corresponding androgen-regulated human ARP26 polypeptide (SEQ ID NO: 18) has 258 residues. Furthermore, the ARP28 cDNA sequence, shown herein as the 1401 nucleotide sequence SEQ ID NO: 19, contains an open reading frame from nucleotides 45 to 1085, which is predicted to encode the 347 amino acid human ARP28 polypeptide (SEQ ID NO: 20) with at least three transmembrane domains. The androgen-regulated ARP30 cDNA has a sequence (SEQ ID NO: 21) of 3318 nucleotides; the human ARP30 polypeptide (SEQ ID NO: 22), a protein of 601 amino acids, is encoded by an open reading frame positioned between nucleotides 252 to 2054 of SEQ ID NO: 21. Furthermore, the androgen-regulated ARP33 cDNA has a nucleic acid sequence (SEQ ID NO: 23) of 1690 nucleotides with an open reading frame from nucleotide 98 to 1313. The human ARP33 polypeptide, a protein of 405 residues shown herein as SEQ ID NO: 24, is predicted to include at least one transmembrane domain. The androgen-regulated ARP11 cDNA has a nucleic acid sequence (SEQ ID NO: 33) of 3067 nucleotides. An open reading frame from nucleotide 790 to 1805 encodes a protein of 338 residues (SEQ ID NO: 34).

ARP6, ARP10, ARP12, ARP18, ARP19, ARP21, ARP22 and ARP29 also are androgen-regulated sequences expressed in prostate. The human ARP6 cDNA sequence is shown herein as a 504 nucleotide sequence (SEQ ID NO: 25); the human ARP10 cDNA sequence is shown herein as a 2189 nucleotide sequence (SEQ ID NO: 26); the human ARP12 cDNA sequence is shown herein as a 2576 nucleotide sequence (SEQ ID NO: 27); and the human ARP18 cDNA sequence is shown herein as a 521 nucleotide sequence (SEQ ID NO: 28). Furthermore, the human ARP19 cDNA sequence is shown herein as a 644 nucleotide sequence (SEQ ID NO: 29); the human ARP21 cDNA sequence is shown herein as a 1460 nucleotide sequence (SEQ ID NO: 30); the human ARP22 cDNA sequence is shown herein as a 774 nucleotide sequence (SEQ ID NO: 31); and the human ARP29 cDNA sequence is shown herein as a 386 nucleotide sequence (SEQ ID NO: 32).

Table 1

Summary of Transmembrane Domains Identified in ARPs

Gene Name	TMPRED*
ARP 7	3 TMs**
ARP 15	3 TMs
ARP 16	8 TMs
ARP 8	0
ARP 9	4 TMs
ARP 13	1 TM
ARP 24	4 TMs
ARP 28	3 TMs
ARP 30	0
ARP 33	1 TM

* TMPRED program at http://www.ch.embnet.org/software/MPRED_form.html is used.

** Either CDS or the largest ORF is used for prediction, so the number of transmembranes (Tms) may be underestimated. Only scores above 500 are considered significant and reported here.

Cells were cultured as follows. LNCaP cells were cultured in RPMI 1640 medium with 5% FBS (Gibco-BRL). For androgen stimulation, six flasks (175 cm^2) of LNCaP cells were starved for androgens by culturing in CS media (RPMI 1640 with 10% charcoal filtered FBS). After 48 hours of incubation, three flasks were incubated with CS media plus cycloheximide (1 µg/µl) and the other three were incubated with CS media plus 1 nM of R1881 and cycloheximide (1µg/µl). All LNCaP cells were incubated for an additional 48 hours and then harvested. For time course experiments, LNCaP cells were

harvested 4, 8, 12, 16, 24, 26, and 48 hours after incubation with R1881 containing media.

Microarray fabrication was performed essentially as follows. The 40 k sequence-verified cDNAs from Research Genetics, Inc., (Huntsville, Alabama) were PCR amplified according to the manufacturer's protocol. PCR products were purified in a 384-well format using MultiScreen PCR clean-up plates (Millipore, Bedford, MA) and verified by agarose gel electrophoresis. PCR products were re-suspended in a 384-well format at a concentration of 0.15 µg/µl in 3X SSC. After arraying the PCR products onto Type VII glass slides (Amersham) at 60% relative humidity and 20°C using a 48-pin printhead on the ChipWriter high-speed robotics system (Virtek; Ontario, CA), arrayed slides were baked at 85°C for two hours and then stored in a dessicator prior to use.

cDNA labeling and hybridization were performed essentially as follows. mRNA (1 µg) or total RNA (30 µg) was mixed with 1 µl of anchored oligo dT primer (Amersham), incubated at 70°C for 10 minutes, and then chilled on ice. Then 4 µl of 5X first strand cDNA synthesis buffer (Gibco-BRL), 2 µl of 0.1 M DTT (Gibco-BRL), 1 µl of HPRI (20 µg/µl) (Amersham), and 1 µl of dNTP mix (Amersham); containing 2mM dATP, 2mM dGTP, 2mM dTTP and 1mM dCTP), 1 µl of Cy3 dCTP (1mM) (Amersham) and 1 µl of SuperScript II RT (200 µg/µl) were added, and the mixture incubated at 42°C for 2 hours. A fter first strand cDNA labeling, the reaction mixture was incubated at 94°C for 3 minutes. Unlabeled RNAs were hybrolyzed by addition of 1 µl of 5N NaOH and incubation at 37°C for 10 minutes. Subsequently, 1 µl of 5M HCl and 5 µl of 1M Tris-HCl (pH 7.5) were added to neutralize the reaction mixture. The mixture was then purified using a Qiagen PCR purification kit (Qiagen) essentially according to

the manufacturer's protocol with two washes with PE buffer; DNA was eluted with 30 µl of dH_2O. The probe was mixed with 1 µl of dA/dT (12-18) (1 µg/µl) (Pharmacia) and 1 µl of human Cot I DNA (1 µg/µl) (Gibco-BRL) denatured at 94°C for 5 minutes. An equal volume of 2X Microarray Hybridization Solution (Amersham) was added, and the mixture was prehybridized at 50°C for 1 hour. After prehybridization, the probe mixture was added to an arrayed slide and covered with a cover slide. Hybridization was performed in a humid chamber at 52°C for 16 hours. After hybridization, the slide was washed once with 1X SSC/ 0.2% SDS at room temperature for 5 minutes on a shaker, twice with 0.1X SSC/ 0.2% SDS at room temperature for 10 minutes, and once with 0.1X SSC at room temperature for 10 minutes. After washing, the slide was rinsed in distilled water to remove trace salts and dried. Hybridized microarray slides were scanned with the ScanArray 5000 (GSI Lumonics) at 10 um resolution.

Hybridization was repeated three times. For the first two hybridizations, RNAs from androgen-stimulated cells were labeled with Cy5 dCTP while RNAs from androgen-starved cells were labeled with Cy3 dCTP. For the third hybridization, RNAs from androgen-stimulated cells were labeled with Cy3 while RNAs from andorgen-starved cells were labeled with Cy5.

Microarray Data Analysis was performed as follows. Each spot on microarray was quantified with the QuantArray software (GSI Lumonics). Data were normalized with the median for each of the four duplicates. Statistical analyses were done using the software VERA and SAM. A lambda value, that describes how likely the gene is differentially expressed, was obtained for each spot on the array.

Northern hybridization was performed as follows. Total RNA (ten µg) was fractionated on 1.2% agarose denaturing gels and transferred to nylon membranes by capillary method (Maniatis). Human and mouse multiple tissue and master blots were purchased from CLONTECH. Blots were hybridized with DNA probes labeled with [alpha-^{32}P]dCTP by random priming using the Rediprime II random primer labeling system (Amersham) according to the manufacturer's protocol. Filters were imaged and quantitated using a phosphor-capture screen and Imagequant software (Molecular Dynamics).

EXAMPLE II

Characterization of ARP15

This example describes preparation of anti-ARP15 antibodies and characterization of ARP15 polypeptide expression.

ARP15 is expressed in patient serum

The coding region of the full-length ARP15 cDNA was cloned into PGEX 4T-1 (Pharmacia). The resulting GST-ARP15 fusion protein was expressed and purified according to the manufacturer's protocols (Pharmacia Inc.) The GST-ARP15 fusion protein was used to immunize mice using a standard protocol. Hybridomas were generated by standard methods and screened by differential ELISA using GST-ARP15 and GST proteins.

Monoclonal hydridomas were generated by limited dilution and screening using ELISA and Western blotting. Several clones were obtained that produced monoclonal antibodies: three clones secreted mAb of IgG1 isotype and one clone secreted mAb of IgG2b isotype. As shown in

Figure 5, monoclonal antibody "1R" detected bands of 32 kd and 16 kd both in a lysate prepared from the LNCaP cell line and in a serum sample from a prostate cancer patient.

Cellular localization of ARP15

Using the anti-ARP15 monoclonal antibody "1R" prepared as described above, cell staining was performed. As shown in Figure 6A, ARP15 was localized to the cell plasma membrane, similar to the expression pattern of β-integrin shown in Figure 6B.

Expression of ARP15 in normal and cancer tissues

Immunohistochemical staining was performed using anti-ARP15 monoclonal antibody 1R against cancerous and normal prostate tissue sections. The immunostaining revealed that ARP15 protein expression was limited to prostate epithelial cells, with little or no expression in stromal cells (see Figure 7). These results are consistent with the Northern analysis showing that ARP15 RNA is predominantly expressed in prostate, testis and ovary tissues.

In sum, these results demonstrate that expression of ARP15 polypeptide, like expression of ARP15 transcripts, is restricted to prostate and a small number of other tissues. These results further demonstrate that the ARP15 polypeptide can be detected in patient serum.

What is claimed is:

1. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP15 binding agent that selectively binds an ARP15 polypeptide;

(b) determining a test expression level of ARP15 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP15 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

2. The method of claim 1, wherein said specimen comprises prostate tissue.

3. The method of claim 1, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

4. The method of claim 1, wherein said ARP15 binding agent that selectively binds said ARP15 polypeptide is an antibody.

5. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP15 nucleic acid molecule;

(b) determining a test expression level of ARP15 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP15 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

6. The method of claim 5, wherein said sample comprises prostate tissue.

7. The method of claim 5, wherein said sample is selected from the group consisting of blood, urine and semen.

8. The method of claim 5, wherein said ARP15 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 3.

9. The method of claim 5, wherein said ARP15 nucleic acid molecule is 15 to 35 nucleotides in length.

10. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP15 regulatory agent.

11. A substantially pure ARP7 nucleic acid molecule, comprising the nucleotide sequence shown as SEQ ID NO: 1.

12. A substantially pure ARP7 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 1-445 of SEQ ID NO: 1.

13. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP7 nucleic acid molecule;

(b) determining a test expression level of ARP7 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP7 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

14. The method of claim 13, wherein said sample comprises prostate tissue.

15. The method of claim 13, wherein said sample is selected from the group consisting of blood, urine and semen.

16. The method of claim 13, wherein said ARP7 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 1.

17. The method of claim 13, wherein said ARP7 nucleic acid molecule is 15 to 35 nucleotides in length.

18. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP7 binding agent that selectively binds an ARP7 polypeptide;

(b) determining a test expression level of ARP7 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP7 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

19. The method of claim 18, wherein said specimen comprises prostate tissue.

20. The method of claim 18, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

21. The method of claim 18, wherein said ARP7 binding agent that selectively binds said ARP7 polypeptide is an antibody.

22. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP7 regulatory agent.

23. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP16 nucleic acid molecule;

(b) determining a test expression level of ARP16 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP16 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

24. The method of claim 23, wherein said sample comprises prostate tissue.

25. The method of claim 23, wherein said sample is selected from the group consisting of blood, urine and semen.

26. The method of claim 23, wherein said ARP16 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 5.

27. The method of claim 23, wherein said ARP16 nucleic acid molecule is 15 to 35 nucleotides in length.

28. A substantially pure ARP16 polypeptide fragment, comprising at least eight contiguous amino acids of residues 26-100 of SEQ ID NO: 6.

29. An ARP16 binding agent, comprising a molecule that selectively binds the ARP16 polypeptide fragment of claim 28.

30. The ARP16 binding agent of claim 29, which is an antibody.

31. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP16 binding agent that selectively binds an ARP16 polypeptide;

(b) determining a test expression level of ARP16 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP16 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

32. The method of claim 31, wherein said specimen comprises prostate tissue.

33. The method of claim 31, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

34. The method of claim 31, wherein said ARP16 binding agent that selectively binds said ARP16 polypeptide is an antibody.

35. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP16 regulatory agent.

36. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP8 nucleic acid molecule;

(b) determining a test expression level of ARP8 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP8 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

37. The method of claim 36, wherein said sample comprises prostate tissue.

38. The method of claim 36, wherein said sample is selected from the group consisting of blood, urine and semen.

39. The method of claim 36, wherein said ARP8 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO:7.

40. The method of claim 36, wherein said ARP8 nucleic acid molecule is 15 to 35 nucleotides in length.

41. A substantially pure ARP8 polypeptide, comprising an amino acid sequence having at least 65% amino acid identity with SEQ ID NO: 8.

42. The substantially pure ARP8 polypeptide of claim 41, comprising the amino acid sequence shown as SEQ ID NO: 8.

43. A substantially pure ARP8 polypeptide fragment, comprising at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8.

44. A substantially pure ARP8 polypeptide fragment, comprising at least eight contiguous amino acids of residues 249-576 of SEQ ID NO: 8.

45. An ARP8 binding agent, comprising a molecule that selectively binds at least eight contiguous amino acids of residues 1-116 of SEQ ID NO: 8.

46. The ARP8 binding agent of claim 45, which is an antibody.

47. An ARP8 binding agent, comprising a molecule that selectively binds at least eight contiguous amino acids of residues 249-576 of SEQ ID NO: 8.

48. The ARP8 binding agent of claim 47, which is an antibody.

49. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP8 binding agent that selectively binds an ARP8 polypeptide;

(b) determining a test expression level of ARP8 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP8 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

50. The method of claim 49, wherein said specimen comprises prostate tissue.

51. The method of claim 49, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

52 The method of claim 49, wherein said ARP8 binding agent that selectively binds said ARP8 polypeptide is an antibody.

53. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP8 regulatory agent.

54. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP9 nucleic acid molecule;

(b) determining a test expression level of ARP9 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP9 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

55. The method of claim 54, wherein said sample comprises prostate tissue.

56. The method of claim 54, wherein said sample is selected from the group consisting of blood, urine and semen.

57. The method of claim 54, wherein said ARP9 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 9.

58. The method of claim 54, wherein said ARP9 nucleic acid molecule is 15 to 35 nucleotides in length.

59. A substantially pure ARP9 polypeptide, comprising an amino acid sequence having at least 65% amino acid identity with SEQ ID NO: 10.

60. The substantially pure ARP9 polypeptide of claim 59, comprising the amino acid sequence shown as SEQ ID NO: 10.

61. A substantially pure ARP9 polypeptide fragment, comprising at least eight contiguous amino acids of residues 1-83 of SEQ ID NO: 10.

62. The substantially pure ARP9 polypeptide fragment of claim 61, comprising at least eight contiguous amino acids of residues 47-62 of SEQ ID NO: 10.

63. An ARP9 binding agent, comprising a molecule that selectively binds at least eight contiguous amino acids of residues 1-83 of SEQ ID NO: 10.

64. The ARP9 binding agent of claim 63, which is an antibody.

65. The ARP9 binding agent of claim 63, comprising a molecule that selectively binds at least eight contiguous amino acids of residues 47-62 of SEQ ID NO: 10.

66. The ARP9 binding agent of claim 65, which is an antibody.

67. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP9 binding agent that selectively binds an ARP9 polypeptide;

(b) determining a test expression level of ARP9 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP9 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

68. The method of claim 67, wherein said specimen comprises prostate tissue.

69. The method of claim 67, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

70. The method of claim 67, wherein said ARP9 binding agent that selectively binds said ARP9 polypeptide is an antibody.

71. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP9 regulatory agent.

72. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP13 nucleic acid molecule;

(b) determining a test expression level of ARP13 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP13 RNA, wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

73. The method of claim 72, wherein said sample comprises prostate tissue.

74. The method of claim 72, wherein said sample is selected from the group consisting of blood, urine and semen.

75. The method of claim 72, wherein said ARP13 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 11.

76. The method of claim 72, wherein said ARP13 nucleic acid molecule is 15 to 35 nucleotides in length.

77. A substantially pure ARP13 polypeptide, comprising an amino acid sequence having at least 90% amino acid identity with SEQ ID NO: 12.

78. The substantially pure ARP13 polypeptide of claim 77, comprising the amino acid sequence shown as SEQ ID NO: 12.

79. A substantially pure ARP13 polypeptide fragment, comprising at least eight contiguous amino acids of SEQ ID NO: 12.

80. An ARP13 binding agent, comprising a molecule that selectively binds at least eight contiguous amino acids of the ARP13 polypeptide SEQ ID NO: 12.

81. The ARP13 binding agent of claim 80, which is an antibody.

82. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP13 binding agent that selectively binds an ARP13 polypeptide;

(b) determining a test expression level of ARP13 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP13 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

83. The method of claim 82, wherein said specimen comprises prostate tissue.

84. The method of claim 82, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

85. The method of claim 82, wherein said ARP13 binding agent that selectively binds said ARP13 polypeptide is an antibody.

86. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP13 regulatory agent.

87. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP20 nucleic acid molecule;

(b) determining a test expression level of ARP20 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP20 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

88. The method of claim 87, wherein said sample comprises prostate tissue.

89. The method of claim 87, wherein said sample is selected from the group consisting of blood, urine and semen.

90. The method of claim 87, wherein said ARP20 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 13.

91. The method of claim 87, wherein said ARP20 nucleic acid molecule is 15 to 35 nucleotides in length.

92. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP20 binding agent that selectively binds an ARP20 polypeptide;

(b) determining a test expression level of ARP20 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP20 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

93. The method of claim 92, wherein said specimen comprises prostate tissue.

94. The method of claim 92, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

95. The method of claim 92, wherein said ARP20 binding agent that selectively binds said ARP20 polypeptide is an antibody.

96. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP20 regulatory agent.

97. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP24 nucleic acid molecule;

(b) determining a test expression level of ARP24 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP24 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

98. The method of claim 97, wherein said sample comprises prostate tissue.

99. The method of claim 97, wherein said sample is selected from the group consisting of blood, urine and semen.

100. The method of claim 97, wherein said ARP24 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 15.

101. The method of claim 97, wherein said ARP24 nucleic acid molecule is 15 to 35 nucleotides in length.

102. A substantially pure ARP24 polypeptide, comprising an amino acid sequence having at least 30% amino acid identity with SEQ ID NO: 16.

103. The substantially pure ARP24 polypeptide of claim 102, comprising the amino acid sequence shown as SEQ ID NO: 16.

104. A substantially pure ARP24 polypeptide fragment, comprising at least eight contiguous amino acids of SEQ ID NO: 16.

105. An ARP24 binding agent, comprising a molecule that selectively binds at least eight contiguous amino acids of the ARP24 polypeptide SEQ ID NO: 16.

106. The ARP24 binding agent of claim 105, which is an antibody.

107. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP24 binding agent that selectively binds an ARP24 polypeptide;

(b) determining a test expression level of ARP24 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP24 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the

presence of a prostate neoplastic condition in said individual.

108. The method of claim 107, wherein said specimen comprises prostate tissue.

109. The method of claim 107, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

110. The method of claim 107, wherein said ARP24 binding agent that selectively binds said ARP24 polypeptide is an antibody.

111. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP24 regulatory agent.

112. A substantially pure ARP26 nucleic acid molecule, comprising the nucleotide sequence shown as SEQ ID NO: 17.

113. A substantially pure ARP26 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 1404-1516 of SEQ ID NO: 17.

114. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP26 nucleic acid molecule;

(b) determining a test expression level of ARP26 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP26 RNA, wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

115. The method of claim 114, wherein said sample comprises prostate tissue.

116. The method of claim 114, wherein said sample is selected from the group consisting of blood, urine and semen.

117. The method of claim 114, wherein said ARP26 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 17.

118. The method of claim 114, wherein said ARP26 nucleic acid molecule is 15 to 35 nucleotides in length.

119. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP26 binding agent that selectively binds an ARP26 polypeptide;

(b) determining a test expression level of ARP26 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP26 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

120. The method of claim 119, wherein said specimen comprises prostate tissue.

121. The method of claim 119, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

122. The method of claim 119, wherein said ARP26 binding agent that selectively binds said ARP26 polypeptide is an antibody.

123. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP26 regulatory agent.

124. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP28 nucleic acid molecule;

(b) determining a test expression level of ARP28 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP28 RNA, wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

125. The method of claim 124, wherein said sample comprises prostate tissue.

126. The method of claim 124, wherein said sample is selected from the group consisting of blood, urine and semen.

127. The method of claim 124, wherein said ARP28 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 19.

128. The method of claim 124, wherein said ARP28 nucleic acid molecule is 15 to 35 nucleotides in length.

129. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP28 binding agent that selectively binds an ARP28 polypeptide;

(b) determining a test expression level of ARP28 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP28 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

130. The method of claim 129, wherein said specimen comprises prostate tissue.

131. The method of claim 129, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

132. The method of claim 129, wherein said ARP28 binding agent that selectively binds said ARP28 polypeptide is an antibody.

133. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP28 regulatory agent.

134. A substantially pure ARP30 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 2346-2796 of SEQ ID NO: 21.

135. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP30 nucleic acid molecule comprising at least 10 contiguous nucleotides of nucleotides 1-1829 or nucleotides 2346-3318 of SEQ ID NO: 21;

(b) determining a test expression level of ARP30 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP30 RNA, wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

136. The method of claim 135, wherein said sample comprises prostate tissue.

137. The method of claim 135, wherein said sample is selected from the group consisting of blood, urine and semen.

138. The method of claim 135, wherein said ARP30 nucleic acid molecule comprises at least 10 contiguous nucleotides of nucleotides 2346-3318 of SEQ ID NO: 21.

139. The method of claim 135, wherein said ARP30 nucleic acid molecule is 15 to 35 nucleotides in length.

140. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP30 binding agent that selectively binds an ARP30 polypeptide;

(b) determining a test expression level of ARP30 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP30 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

141. The method of claim 140, wherein said specimen comprises prostate tissue.

142. The method of claim 140, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

143. The method of claim 140, wherein said ARP30 binding agent that selectively binds said ARP30 polypeptide is an antibody.

144. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP30 regulatory agent.

145. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP33 nucleic acid molecule;

(b) determining a test expression level of ARP33 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP33 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

146. The method of claim 145, wherein said sample comprises prostate tissue.

147. The method of claim 145, wherein said sample is selected from the group consisting of blood, urine and semen.

148. The method of claim 145, wherein said ARP33 nucleic acid molecule comprises at least 10 contiguous nucleotides of SEQ ID NO: 23.

149. The method of claim 145, wherein said ARP33 nucleic acid molecule is 15 to 35 nucleotides in length.

150. A substantially pure ARP33 polypeptide, comprising an amino acid sequence having at least 70% amino acid identity with SEQ ID NO: 24.

151. The substantially pure ARP33 polypeptide of claim 150, comprising the amino acid sequence shown as SEQ ID NO: 24.

152. A substantially pure ARP33 polypeptide fragment, comprising at least eight contiguous amino acids of residues 1-132 or 251-405 of SEQ ID NO: 24.

153. An ARP33 binding agent, comprising a molecule that selectively binds at least eight contiguous amino acids of residues 1-132 or 251-405 of SEQ ID NO: 24.

154. The ARP33 binding agent of claim 153, which is an antibody.

155. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP33 binding agent that selectively binds an ARP33 polypeptide;

(b) determining a test expression level of ARP33 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP33 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the

presence of a prostate neoplastic condition in said individual.

156. The method of claim 155, wherein said specimen comprises prostate tissue.

157. The method of claim 155, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

158. The method of claim 155, wherein said ARP33 binding agent that selectively binds said ARP33 polypeptide is an antibody.

159. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP33 regulatory agent.

160. A substantially pure ARP6 nucleic acid molecule, comprising the nucleotide sequence shown as SEQ ID NO: 25.

161. A substantially pure ARP6 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 505-526 of SEQ ID NO: 25.

162. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP6 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 25;

(b) determining a test expression level of ARP6 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP6 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

163. The method of claim 162, wherein said sample comprises prostate tissue.

164. The method of claim 162, wherein said sample is selected from the group consisting of blood, urine and semen.

165. The method of claim 162, wherein said ARP6 nucleic acid molecule is 15 to 35 nucleotides in length.

166. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP6 regulatory agent.

167. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP10 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 26;

(b) determining a test expression level of ARP10 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP10 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

168. The method of claim 167, wherein said sample comprises prostate tissue.

169. The method of claim 167, wherein said sample is selected from the group consisting of blood, urine and semen.

170. The method of claim 167, wherein said ARP10 nucleic acid molecule is 15 to 35 nucleotides in length.

171. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP10 regulatory agent.

172. A substantially pure ARP12 nucleic acid molecule, comprising the nucleotide sequence shown as SEQ ID NO: 27.

173. A substantially pure ARP12 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 1635-1659 of SEQ ID NO: 27.

174. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP12 nucleic acid molecule comprising at least 10 contiguous nucleotides of nucleotides 1-1659 of SEQ ID NO: 27;

(b) determining a test expression level of ARP12 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP12 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

175. The method of claim 174, wherein said sample comprises prostate tissue.

176. The method of claim 174, wherein said sample is selected from the group consisting of blood, urine and semen.

177. The method of claim 174, wherein said ARP12 nucleic acid molecule is 15 to 35 nucleotides in length.

178. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP12 regulatory agent.

179. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP18 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 28;

(b) determining a test expression level of ARP18 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP18 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

180. The method of claim 179, wherein said sample comprises prostate tissue.

181. The method of claim 179, wherein said sample is selected from the group consisting of blood, urine and semen.

182. The method of claim 179, wherein said ARP18 nucleic acid molecule is 15 to 35 nucleotides in length.

183. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP18 regulatory agent.

184. A substantially pure ARP19 nucleic acid molecule, comprising the nucleotide sequence shown as SEQ ID NO: 29.

185. A substantially pure ARP19 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 1-31 or 478-644 of SEQ ID NO: 29.

186. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP19 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 29;

(b) determining a test expression level of ARP19 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP19 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

187. The method of claim 186, wherein said sample comprises prostate tissue.

188. The method of claim 186, wherein said sample is selected from the group consisting of blood, urine and semen.

189. The method of claim 186, wherein said ARP19 nucleic acid molecule is 15 to 35 nucleotides in length.

190. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP19 regulatory agent.

191. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP21 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 30;

(b) determining a test expression level of ARP21 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP21 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

192. The method of claim 191, wherein said sample comprises prostate tissue.

193. The method of claim 191, wherein said sample is selected from the group consisting of blood, urine and semen.

194. The method of claim 191, wherein said ARP21 nucleic acid molecule is 15 to 35 nucleotides in length.

195. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP21 regulatory agent.

196. A substantially pure ARP22 nucleic acid molecule, comprising the nucleotide sequence shown as SEQ ID NO: 31.

197. A substantially pure ARP22 nucleic acid molecule, comprising at least 10 contiguous nucleotides of nucleotides 1-73 or 447-464 of SEQ ID NO: 31.

198. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP22 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 31;

(b) determining a test expression level of ARP22 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP22 RNA,

wherein an altered test expression level as compared to said control expression level indicates the

presence of a prostate neoplastic condition in said individual.

199. The method of claim 198, wherein said sample comprises prostate tissue.

200. The method of claim 198, wherein said sample is selected from the group consisting of blood, urine and semen.

201. The method of claim 198, wherein said ARP22 nucleic acid molecule comprises at least 10 contiguous nucleotides of nucleotides 1-73 or 447-464 of SEQ ID NO: 31.

202. The method of claim 198, wherein said ARP22 nucleic acid molecule is 15 to 35 nucleotides in length.

203. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP22 regulatory agent.

204. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a sample from said individual with an ARP29 nucleic acid molecule comprising at least 10 contiguous nucleotides of SEQ ID NO: 32;

(b) determining a test expression level of ARP29 RNA in said sample; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP29 RNA,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

205. The method of claim 204, wherein said sample comprises prostate tissue.

206. The method of claim 204, wherein said sample is selected from the group consisting of blood, urine and semen.

207. The method of claim 204, wherein said ARP29 nucleic acid molecule is 15 to 35 nucleotides in length.

208. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP29 regulatory agent.

209. A method of diagnosing or predicting susceptibility to a prostate neoplastic condition in an individual, comprising:

(a) contacting a specimen from said individual with an ARP11 binding agent that selectively binds an ARP11 polypeptide;

(b) determining a test expression level of ARP11 polypeptide in said specimen; and

(c) comparing said test expression level to a non-neoplastic control expression level of ARP11 polypeptide,

wherein an altered test expression level as compared to said control expression level indicates the presence of a prostate neoplastic condition in said individual.

210. The method of claim 209, wherein said specimen comprises prostate tissue.

211. The method of claim 209, wherein said specimen is selected from the group consisting of blood, serum, urine and semen.

212. The method of claim 209, wherein said ARP11 binding agent that selectively binds said ARP11 polypeptide is an antibody.

213. A method for treating or reducing the severity of a prostate neoplastic condition in an individual, comprising administering to said individual an ARP11 regulatory agent.

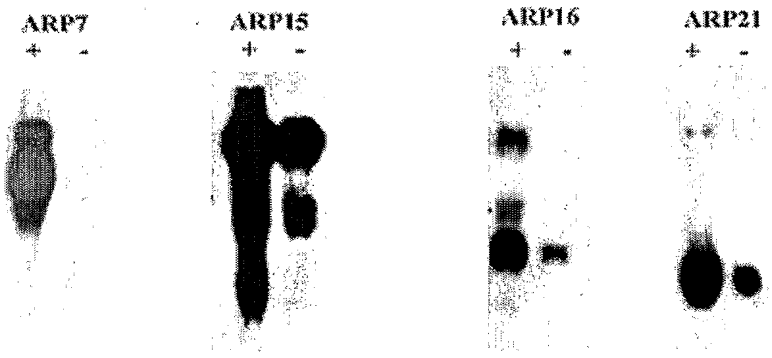
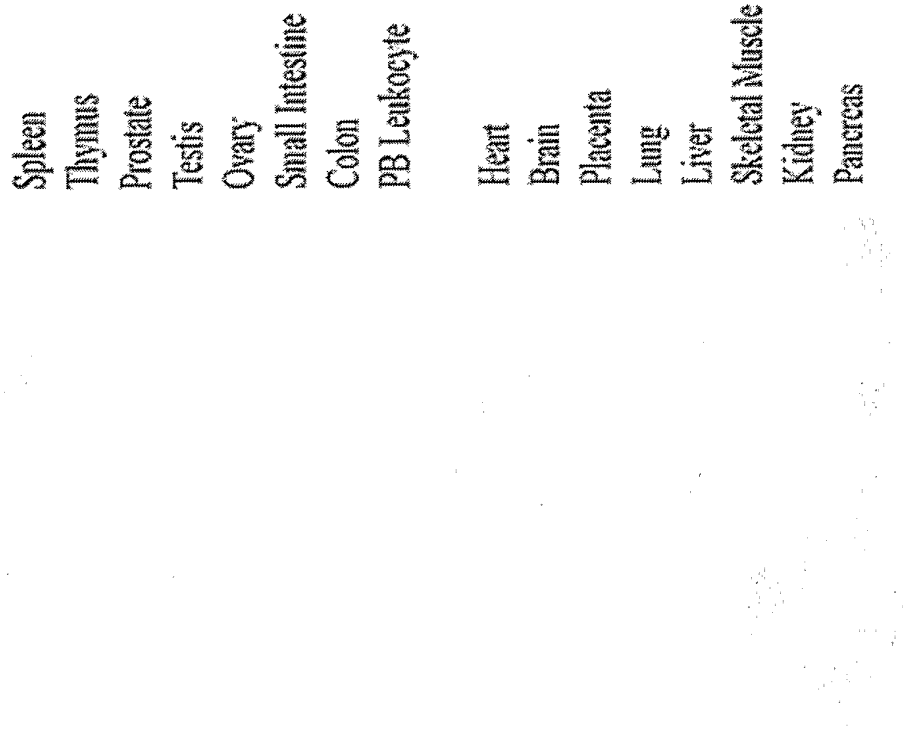
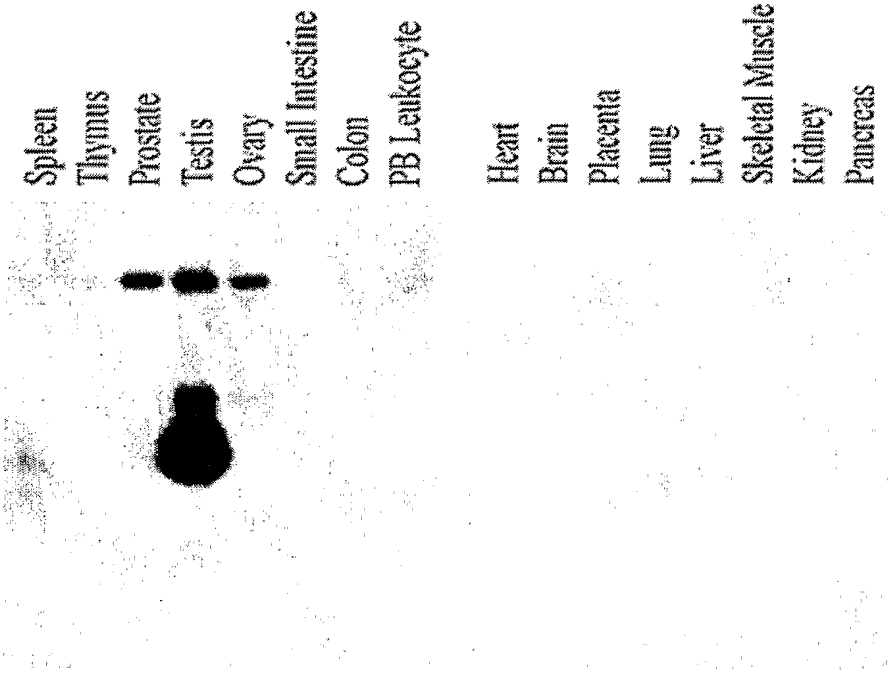


FIGURE 1



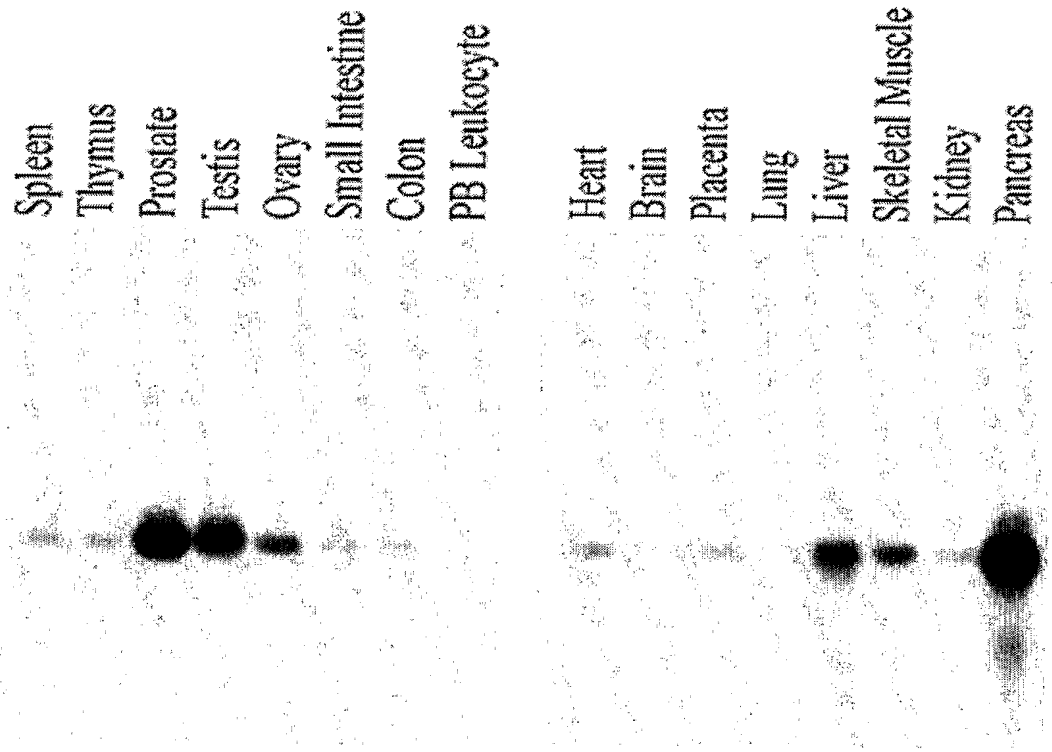
ARP7 MTN hybridization

FIGURE 2



ARP15 MTN hybridization

FIGURE 3



ARP21 MTN hybridization

FIGURE 4

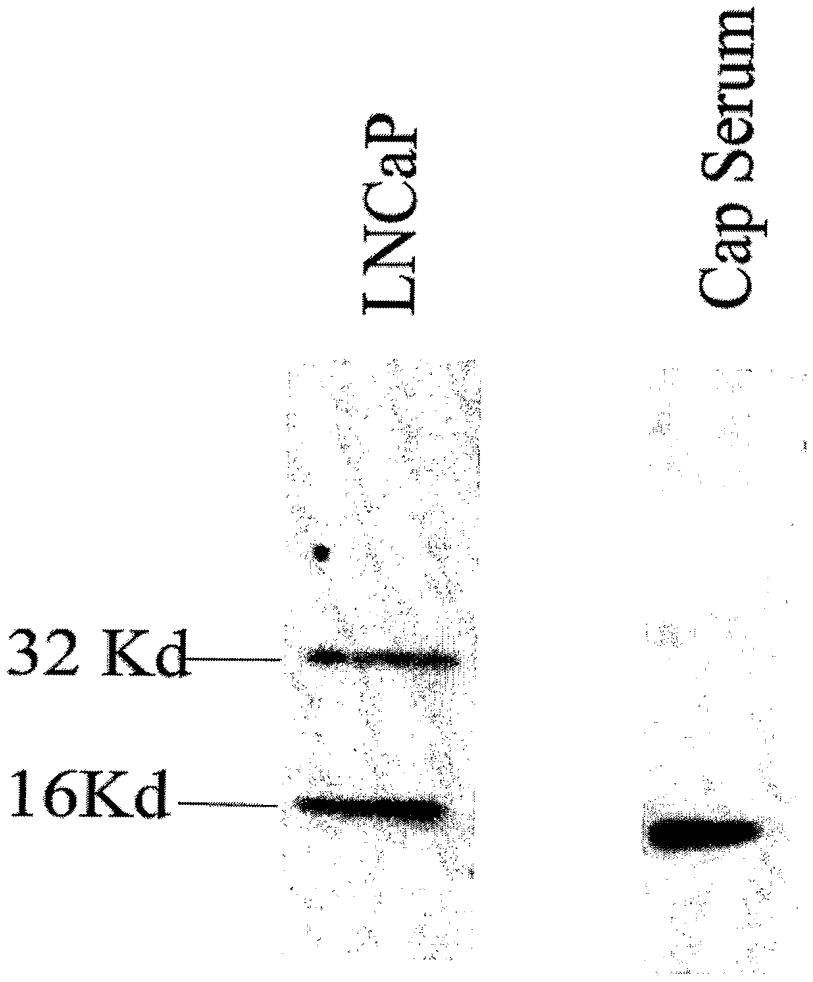
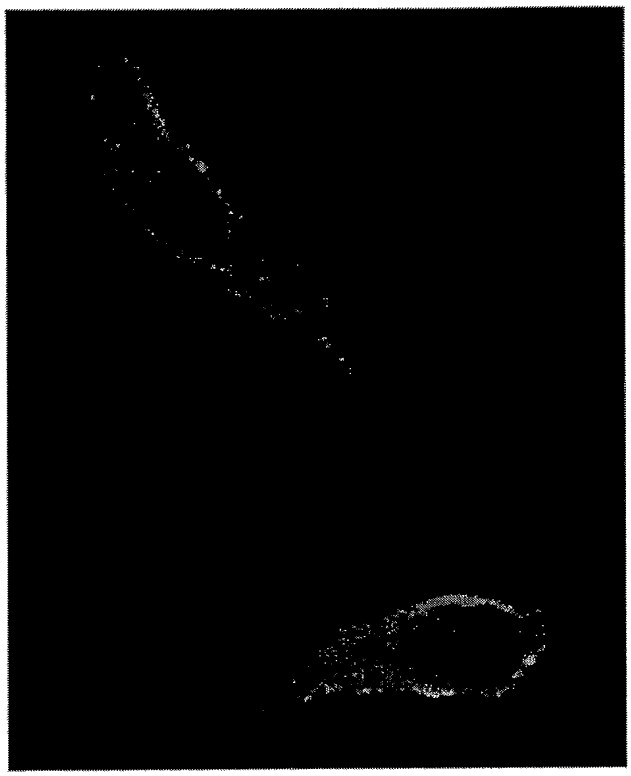


FIGURE 5

A:



B:

FIGURE 6

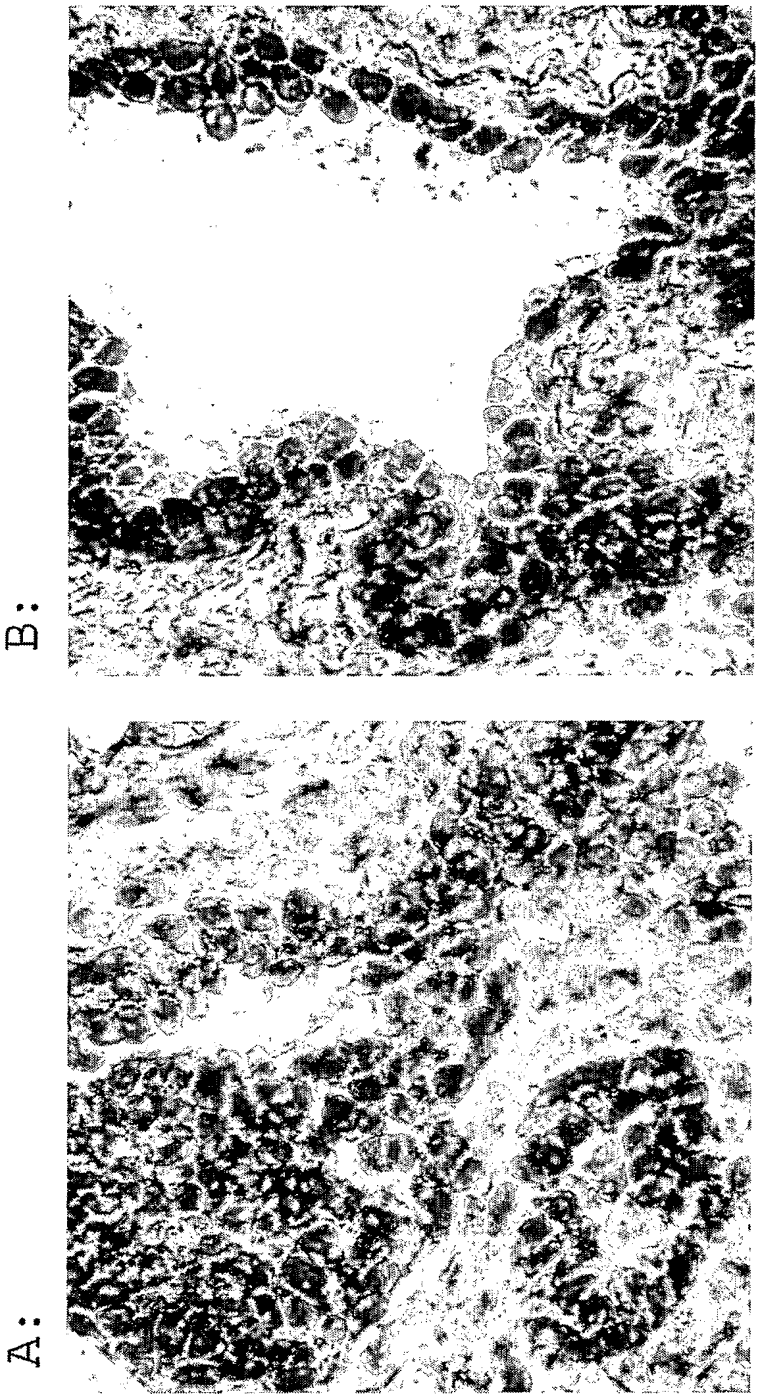


FIGURE 7

SEQUENCE LISTING

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Lin, Biaoyang

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35 40 45

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Gly Leu Ala Ala Phe Thr Lys Leu Tyr Glu Ser Leu Leu Pro Phe Ala
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act gga gaa cat gga tct atg gag agt atc tgg acc ttc ttc att gag   716
Thr Gly Glu His Gly Ser Met Glu Ser Ile Trp Thr Phe Phe Ile Glu
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aac aat gtt tcc cat agt aca ctg gtg gca ttg ttc tat cat ttt gtt   764
Asn Asn Val Ser His Ser Thr Leu Val Ala Leu Phe Tyr His Phe Val
            85                  90                  95

caa ata gtt cat aag aag aat gtc agt gta cag tat cga gaa tat ggc   812
Gln Ile Val His Lys Lys Asn Val Ser Val Gln Tyr Arg Glu Tyr Gly
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Leu His Ala Ala Gly Leu Tyr Phe Leu Leu Leu Glu Val Pro Gly Ser
    115                 120                 125

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Val Ala Asn Gln Val Phe His Pro Val Met Phe Asp Lys Cys Ile Gln
130                 135                 140                 145

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Thr Leu Lys Lys Ser Trp Pro Gln Glu Ser Asn Leu Asn Arg Lys Arg
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Lys Lys Glu Gln Pro Lys Ser Ser Gln Ala Asn Pro Gly Arg His Arg
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Lys Arg Gly Lys Pro Pro Arg Arg Glu Asp Ile Glu Met Asp Glu Ile
        180                 185                 190

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Ile Glu Glu Gln Glu Asp Glu Asn Ile Cys Phe Ser Ala Arg Asp Leu
    195                 200                 205

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Leu Leu Pro Lys Phe Ser Leu Lys Glu Lys Pro Gln Cys Val Gln Asn
                230                 235                 240

tgt ata gag gtc ttt gtt tca tta act aat ttt gag cca gtt ctt cat  1244
Cys Ile Glu Val Phe Val Ser Leu Thr Asn Phe Glu Pro Val Leu His
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290                 295                 300                 305

gta ata tta atg tta gaa gtt ggt gaa gga tcc cat cgt gcc ccc ctt   1436
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                310                 315                 320

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Ala Val Thr Ser Gln Val Ile Asn Cys Arg Asn Gln Ala Val Gln Phe
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Ile Ser Ala Leu Val Asp Glu Leu Lys Glu Ser Ile Phe Pro Val Val
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Arg Ile Leu Leu Gln His Ile Cys Ala Lys Val Val Asp Lys Ser Glu
    355                 360                 365

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Tyr Arg Thr Phe Ala Ala Gln Ser Leu Val Gln Leu Leu Ser Lys Leu
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Pro Cys Gly Glu Tyr Ala Met Phe Ile Ala Trp Leu Tyr Lys Tyr Ser
                390                 395                 400

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Arg Ser Ser Lys Ile Pro His Arg Val Phe Thr Leu Asp Val Val Leu
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Phe Asp Arg Cys Leu Asp Lys Ala Pro Thr Val Arg Ser Lys Ala Leu
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530                 535                 540                 545

ctg aga agg agg atc agg gat gag aag acc aac gtt agg aag tct gca   2156
Leu Arg Arg Arg Ile Arg Asp Glu Lys Thr Asn Val Arg Lys Ser Ala
                550                 555                 560

ctg cag gta tta gtg agt att ctg aaa cac tgt gat gtc tca ggc atg   2204
Leu Gln Val Leu Val Ser Ile Leu Lys His Cys Asp Val Ser Gly Met
            565                 570                 575

aag gaa gac ctg tgg att ctg cag gac cag tgt cgg gac cct gca gtg   2252
Lys Glu Asp Leu Trp Ile Leu Gln Asp Gln Cys Arg Asp Pro Ala Val
        580                 585                 590

tct gtc cgg aag cag gcc ctc cag tct ctt act gaa ctc ctt atg gct   2300
Ser Val Arg Lys Gln Ala Leu Gln Ser Leu Thr Glu Leu Leu Met Ala
    595                 600                 605

cag cct aga tgc gtg cag atc cag aaa gcc tgg ttg cgg ggg gtg gtc   2348
Gln Pro Arg Cys Val Gln Ile Gln Lys Ala Trp Leu Arg Gly Val Val
610                 615                 620                 625

ccg gtg gtg atg gac tgc gag agc act gtg cag gag aag gcc ctg gag   2396
Pro Val Val Met Asp Cys Glu Ser Thr Val Gln Glu Lys Ala Leu Glu
                630                 635                 640

ttc ctg gac cag ctg ctg ctg cag aac atc cgg cat cac agt cat ttt   2444
Phe Leu Asp Gln Leu Leu Leu Gln Asn Ile Arg His His Ser His Phe
            645                 650                 655

cac tct ggg gac gac agc cag gtc ctc gcc tgg gcg ctt ctt act ctc   2492
His Ser Gly Asp Asp Ser Gln Val Leu Ala Trp Ala Leu Leu Thr Leu
        660                 665                 670

ctc acc acc gaa agc cag gaa ctg agc cga tat tta aat aag gct ttt   2540
Leu Thr Thr Glu Ser Gln Glu Leu Ser Arg Tyr Leu Asn Lys Ala Phe
    675                 680                 685

cat atc tgg tcc aag aaa gaa aaa ttc tca ccc act ttt ata aac aat   2588
His Ile Trp Ser Lys Lys Glu Lys Phe Ser Pro Thr Phe Ile Asn Asn
690                 695                 700                 705
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gta ata tct cac act ggc acg gaa cat tcg gca cct gcc tgg atg ctg   2636
Val Ile Ser His Thr Gly Thr Glu His Ser Ala Pro Ala Trp Met Leu
                710                 715                 720

ctc tcc aag att gct ggc tcc tca ccc agg ctg gac tac agc aga ata   2684
Leu Ser Lys Ile Ala Gly Ser Ser Pro Arg Leu Asp Tyr Ser Arg Ile
            725                 730                 735

ata caa tct tgg gag aaa atc agc agt cag cag aat ccc aat tca aac   2732
Ile Gln Ser Trp Glu Lys Ile Ser Ser Gln Gln Asn Pro Asn Ser Asn
        740                 745                 750

acc tta gga cat att ctc tgt gtg att ggg cat att gca aag cat ctt   2780
Thr Leu Gly His Ile Leu Cys Val Ile Gly His Ile Ala Lys His Leu
    755                 760                 765

cct aag agc acc cgg gac aaa gtg act gat gct gtc aag tgt aag ctg   2828
Pro Lys Ser Thr Arg Asp Lys Val Thr Asp Ala Val Lys Cys Lys Leu
770                 775                 780                 785

aat gga ttt cag tgg tct cta gag gtg atc agt tca gct gtt gac gcc   2876
Asn Gly Phe Gln Trp Ser Leu Glu Val Ile Ser Ser Ala Val Asp Ala
                790                 795                 800

ttg cag agg ctt tgt aga gca tct gca gag aca cca gca gag gag cag   2924
Leu Gln Arg Leu Cys Arg Ala Ser Ala Glu Thr Pro Ala Glu Glu Gln
            805                 810                 815

gaa ttg ctg acg cag gtg tgt ggg gat gta ctc tcc acc tgc gag cac   2972
Glu Leu Leu Thr Gln Val Cys Gly Asp Val Leu Ser Thr Cys Glu His
        820                 825                 830

cgc ctc tcc aac atc gtt ctc aag gag aat gga aca ggg aat atg gac   3020
Arg Leu Ser Asn Ile Val Leu Lys Glu Asn Gly Thr Gly Asn Met Asp
    835                 840                 845

gaa gac ctg ttg gtg aag tac att ttt acc tta ggg gat ata gcc cag   3068
Glu Asp Leu Leu Val Lys Tyr Ile Phe Thr Leu Gly Asp Ile Ala Gln
850                 855                 860                 865

ctg tgt cca gcc agg gtg gag aag cgc atc ttc ctt ctg att cag tcc   3116
Leu Cys Pro Ala Arg Val Glu Lys Arg Ile Phe Leu Leu Ile Gln Ser
                870                 875                 880

gtc ctg gct tcg tct gct gat gct gac cac tca cca tca tct caa ggc   3164
Val Leu Ala Ser Ser Ala Asp Ala Asp His Ser Pro Ser Ser Gln Gly
            885                 890                 895

agc agt gag gcc cca gcg tct cag cca ccc ccc cag gtc aga ggt tct   3212
Ser Ser Glu Ala Pro Ala Ser Gln Pro Pro Pro Gln Val Arg Gly Ser
        900                 905                 910

gtc atg ccc tct gtg att aga gca cat gcc atc att acc tta ggt aag   3260
Val Met Pro Ser Val Ile Arg Ala His Ala Ile Ile Thr Leu Gly Lys
    915                 920                 925
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ctg tgc tta cag cac gag gat ctg gca aag aag agc atc cca gcc ctg   3308
Leu Cys Leu Gln His Glu Asp Leu Ala Lys Lys Ser Ile Pro Ala Leu
930                 935                 940                 945

gtg cga gag ctc gag gtg tgt gag gac gtg gct gtc cgc aac aac gtc   3356
Val Arg Glu Leu Glu Val Cys Glu Asp Val Ala Val Arg Asn Asn Val
                950                 955                 960

atc att gta atg tgc gat ctc tgc att cgc tac acc atc atg gtg gac   3404
Ile Ile Val Met Cys Asp Leu Cys Ile Arg Tyr Thr Ile Met Val Asp
            965                 970                 975

aag tat att ccc aac atc tcc atg tgt ctg aag gat tcc gac cca ttc   3452
Lys Tyr Ile Pro Asn Ile Ser Met Cys Leu Lys Asp Ser Asp Pro Phe
        980                 985                 990

atc cgg aag cag aca ctc atc ttg ctt acc aat ctc ttg cag gag gaa   3500
Ile Arg Lys Gln Thr Leu Ile Leu Leu Thr Asn Leu Leu Gln Glu Glu
    995                 1000                1005

ttt gtg aaa tgg aag ggc tcc ctg ttc ttc cga ttt gtc agc act ctg   3548
Phe Val Lys Trp Lys Gly Ser Leu Phe Phe Arg Phe Val Ser Thr Leu
1010                1015                1020                1025

atc gat tca cac cca gac att gcc agc ttc ggg gag ttt tgc ctg gct   3596
Ile Asp Ser His Pro Asp Ile Ala Ser Phe Gly Glu Phe Cys Leu Ala
                1030                1035                1040

cac ctg tta ctg aag agg aac cct gtc atg ttc ttc caa cac ttc att   3644
His Leu Leu Leu Lys Arg Asn Pro Val Met Phe Phe Gln His Phe Ile
            1045                1050                1055

gaa tgt att ttt cac ttt aat aac tat gag aag cat gag aag tac aac   3692
Glu Cys Ile Phe His Phe Asn Asn Tyr Glu Lys His Glu Lys Tyr Asn
        1060                1065                1070

aag ttc ccc cag tca gag aga gag aag cgg ctg ttt tca ttg aag gga   3740
Lys Phe Pro Gln Ser Glu Arg Glu Lys Arg Leu Phe Ser Leu Lys Gly
    1075                1080                1085

aag tca aac aaa gag aga cga atg aaa atc tac aaa ttt ctt cta gag   3788
Lys Ser Asn Lys Glu Arg Arg Met Lys Ile Tyr Lys Phe Leu Leu Glu
1090                1095                1100                1105

cac ttc aca gat gaa cag cga ttc aac atc act tcc aaa atc tgc ctt   3836
His Phe Thr Asp Glu Gln Arg Phe Asn Ile Thr Ser Lys Ile Cys Leu
                1110                1115                1120

agt att ttg gcg tgc ttt gct gat ggc atc cta ccc ctg gac ctg gac   3884
Ser Ile Leu Ala Cys Phe Ala Asp Gly Ile Leu Pro Leu Asp Leu Asp
            1125                1130                1135

gcc agt gag tta ctc tca gac acg ttt gag gtc ctc agc tca aag gag   3932
Ala Ser Glu Leu Leu Ser Asp Thr Phe Glu Val Leu Ser Ser Lys Glu
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        1140                1145                1150

atc aag ctt ttg gca atg aga tct aaa cca gac aaa gac ctc ctt atg   3980
Ile Lys Leu Leu Ala Met Arg Ser Lys Pro Asp Lys Asp Leu Leu Met
    1155                1160                1165

gaa gaa gat gac atg gcc ttg gca aat gta gtc atg cag gaa gct cag   4028
Glu Glu Asp Asp Met Ala Leu Ala Asn Val Val Met Gln Glu Ala Gln
1170                1175                1180                1185

aag aag ctc atc tca caa gtt cag aag agg aat ttc ata gaa aat att   4076
Lys Lys Leu Ile Ser Gln Val Gln Lys Arg Asn Phe Ile Glu Asn Ile
                1190                1195                1200

att cca att atc atc tcc ctg aag act gtg ctg gag aaa aat aag atc   4124
Ile Pro Ile Ile Ile Ser Leu Lys Thr Val Leu Glu Lys Asn Lys Ile
            1205                1210                1215

cca gct ttg cgg gaa ctc atg cac tat ctc agg gag gtg atg cag gat   4172
Pro Ala Leu Arg Glu Leu Met His Tyr Leu Arg Glu Val Met Gln Asp
        1220                1225                1230

tac cga gat gag ctc aag gac ttc ttt gca gtt gac aaa cag ctg gca   4220
Tyr Arg Asp Glu Leu Lys Asp Phe Phe Ala Val Asp Lys Gln Leu Ala
    1235                1240                1245

tca gag ctt gag tat gac atg aag aag tac cag gaa cag ctg gtc cag   4268
Ser Glu Leu Glu Tyr Asp Met Lys Lys Tyr Gln Glu Gln Leu Val Gln
1250                1255                1260                1265

gag cag gag cta gca aaa cat gca gat gtg gcc ggg acg gct gga ggt   4316
Glu Gln Glu Leu Ala Lys His Ala Asp Val Ala Gly Thr Ala Gly Gly
                1270                1275                1280

gct gag gtg gca cct gtg gca cag gtt gcc ctg tgt tta gaa aca gtg   4364
Ala Glu Val Ala Pro Val Ala Gln Val Ala Leu Cys Leu Glu Thr Val
            1285                1290                1295

cca gtt cct gct ggc caa gaa aac cct gcc atg tca cct gcc gtg agc   4412
Pro Val Pro Ala Gly Gln Glu Asn Pro Ala Met Ser Pro Ala Val Ser
        1300                1305                1310

cag ccc tgc aca ccc agg gca agt gct ggc cat gta gca gta tca tct   4460
Gln Pro Cys Thr Pro Arg Ala Ser Ala Gly His Val Ala Val Ser Ser
    1315                1320                1325

cct aca cct gaa aca ggg cca ttg cag agg ttg ctg ccc aaa gcc agg   4508
Pro Thr Pro Glu Thr Gly Pro Leu Gln Arg Leu Leu Pro Lys Ala Arg
1330                1335                1340                1345

ccc atg tcc ctg agc acc att gca atc ctg aat tct gtc aag aaa gcc   4556
Pro Met Ser Leu Ser Thr Ile Ala Ile Leu Asn Ser Val Lys Lys Ala
                1350                1355                1360

gtg gag tca aag agc agg cat cgg agt cgg agc tta gga gtg ctg cct   4604
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Val Glu Ser Lys Ser Arg His Arg Ser Arg Ser Leu Gly Val Leu Pro
            1365                1370                1375

ttc act tta aat tct gga agc cca gaa aaa acg tgc agt cag gtg tct   4652
Phe Thr Leu Asn Ser Gly Ser Pro Glu Lys Thr Cys Ser Gln Val Ser
        1380                1385                1390

tca tac agt ttg gag caa gag tcg aat ggc gag att gag cac gtg acc   4700
Ser Tyr Ser Leu Glu Gln Glu Ser Asn Gly Glu Ile Glu His Val Thr
    1395                1400                1405

aag cgg gcc atc agc acc ccc gag aag agc atc agt gat gtc acg ttt   4748
Lys Arg Ala Ile Ser Thr Pro Glu Lys Ser Ile Ser Asp Val Thr Phe
1410                1415                1420                1425

gga gca ggg gtc agt tac atc ggg aca cca cgg act ccg tcg tca gcc   4796
Gly Ala Gly Val Ser Tyr Ile Gly Thr Pro Arg Thr Pro Ser Ser Ala
                1430                1435                1440

aaa gag aaa att gaa ggc cgg agt caa gga aat gac atc tta tgt tta   4844
Lys Glu Lys Ile Glu Gly Arg Ser Gln Gly Asn Asp Ile Leu Cys Leu
            1445                1450                1455

tca ctg cct gat aaa ccg ccc cca cag cct cag cag tgg aat gtg cgg   4892
Ser Leu Pro Asp Lys Pro Pro Pro Gln Pro Gln Gln Trp Asn Val Arg
        1460                1465                1470

tct ccc gcc agg aat aaa gac act cca gcc tgc agc agg agg tcc ctc   4940
Ser Pro Ala Arg Asn Lys Asp Thr Pro Ala Cys Ser Arg Arg Ser Leu
    1475                1480                1485

cga aag acc cct ctg aaa aca gcc aac taaacagcgc ctcccaccag         4987
Arg Lys Thr Pro Leu Lys Thr Ala Asn
1490                1495

tgtccaggca ggcaggagcc cttgaggaag cagtctcgtg tcctccgtgt gaaggcagct 5047
ggatcacttc ccgcagtcct tgggcagcgc tttgctgtgg aacacgagag ctcctcctca 5107
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catattttcc catctgtaat gacgaaattt tgattctaat atttttttcta ttatttataa 5407
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cag                                                               5470

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Leu Asp Leu Arg Leu Glu Trp Val Asp Thr Val Trp Glu Leu Asp Phe
            20                  25                  30
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Thr Glu Thr Glu Pro Leu Asp Pro Ser Ile Glu Ala Glu Ile Ile Glu
        35                  40                  45
Thr Gly Leu Ala Ala Phe Thr Lys Leu Tyr Glu Ser Leu Leu Pro Phe
    50                  55                  60
Ala Thr Gly Glu His Gly Ser Met Glu Ser Ile Trp Thr Phe Phe Ile
65                  70                  75                  80
Glu Asn Asn Val Ser His Ser Thr Leu Val Ala Leu Phe Tyr His Phe
                85                  90                  95
Val Gln Ile Val His Lys Lys Asn Val Ser Val Gln Tyr Arg Glu Tyr
            100                 105                 110
Gly Leu His Ala Ala Gly Leu Tyr Phe Leu Leu Leu Glu Val Pro Gly
        115                 120                 125
Ser Val Ala Asn Gln Val Phe His Pro Val Met Phe Asp Lys Cys Ile
    130                 135                 140
Gln Thr Leu Lys Lys Ser Trp Pro Gln Glu Ser Asn Leu Asn Arg Lys
145                 150                 155                 160
Arg Lys Lys Glu Gln Pro Lys Ser Ser Gln Ala Asn Pro Gly Arg His
                165                 170                 175
Arg Lys Arg Gly Lys Pro Pro Arg Arg Glu Asp Ile Glu Met Asp Glu
            180                 185                 190
Ile Ile Glu Glu Gln Glu Asp Glu Asn Ile Cys Phe Ser Ala Arg Asp
        195                 200                 205
Leu Ser Gln Ile Arg Asn Ala Ile Phe His Leu Leu Lys Asn Phe Leu
    210                 215                 220
Arg Leu Leu Pro Lys Phe Ser Leu Lys Glu Lys Pro Gln Cys Val Gln
225                 230                 235                 240
Asn Cys Ile Glu Val Phe Val Ser Leu Thr Asn Phe Glu Pro Val Leu
                245                 250                 255
His Glu Cys His Val Thr Gln Ala Arg Ala Leu Asn Gln Ala Lys Tyr
            260                 265                 270
Ile Pro Glu Leu Ala Tyr Tyr Gly Leu Tyr Leu Leu Cys Ser Pro Ile
        275                 280                 285
His Gly Glu Gly Asp Lys Val Ile Ser Cys Val Phe His Gln Met Leu
    290                 295                 300
Ser Val Ile Leu Met Leu Glu Val Gly Glu Gly Ser His Arg Ala Pro
305                 310                 315                 320
Leu Ala Val Thr Ser Gln Val Ile Asn Cys Arg Asn Gln Ala Val Gln
                325                 330                 335
Phe Ile Ser Ala Leu Val Asp Glu Leu Lys Glu Ser Ile Phe Pro Val
            340                 345                 350
Val Arg Ile Leu Leu Gln His Ile Cys Ala Lys Val Val Asp Lys Ser
        355                 360                 365
Glu Tyr Arg Thr Phe Ala Ala Gln Ser Leu Val Gln Leu Leu Ser Lys
    370                 375                 380
Leu Pro Cys Gly Glu Tyr Ala Met Phe Ile Ala Trp Leu Tyr Lys Tyr
385                 390                 395                 400
Ser Arg Ser Ser Lys Ile Pro His Arg Val Phe Thr Leu Asp Val Val
                405                 410                 415
Leu Ala Leu Leu Glu Leu Pro Glu Arg Glu Val Asp Asn Thr Leu Ser
            420                 425                 430
Leu Glu His Gln Lys Phe Leu Lys His Lys Phe Leu Val Gln Glu Ile
        435                 440                 445
Met Phe Asp Arg Cys Leu Asp Lys Ala Pro Thr Val Arg Ser Lys Ala
    450                 455                 460
Leu Ser Ser Phe Ala His Cys Leu Glu Leu Thr Val Thr Ser Ala Ser
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465                 470                 475                 480
Glu Ser Ile Leu Glu Leu Leu Ile Asn Ser Pro Thr Phe Ser Val Ile
                485                 490                 495
Glu Ser His Pro Gly Thr Leu Leu Arg Asn Ser Ser Ala Phe Ser Tyr
            500                 505                 510
Gln Arg Gln Thr Ser Asn Arg Ser Glu Pro Ser Gly Glu Ile Asn Ile
        515                 520                 525
Asp Ser Ser Gly Glu Thr Val Gly Ser Gly Glu Arg Cys Val Met Ala
    530                 535                 540
Met Leu Arg Arg Arg Ile Arg Asp Glu Lys Thr Asn Val Arg Lys Ser
545                 550                 555                 560
Ala Leu Gln Val Leu Val Ser Ile Leu Lys His Cys Asp Val Ser Gly
                565                 570                 575
Met Lys Glu Asp Leu Trp Ile Leu Gln Asp Gln Cys Arg Asp Pro Ala
            580                 585                 590
Val Ser Val Arg Lys Gln Ala Leu Gln Ser Leu Thr Glu Leu Leu Met
        595                 600                 605
Ala Gln Pro Arg Cys Val Gln Ile Gln Lys Ala Trp Leu Arg Gly Val
    610                 615                 620
Val Pro Val Val Met Asp Cys Glu Ser Thr Val Gln Glu Lys Ala Leu
625                 630                 635                 640
Glu Phe Leu Asp Gln Leu Leu Leu Gln Asn Ile Arg His His Ser His
                645                 650                 655
Phe His Ser Gly Asp Asp Ser Gln Val Leu Ala Trp Ala Leu Leu Thr
            660                 665                 670
Leu Leu Thr Thr Glu Ser Gln Glu Leu Ser Arg Tyr Leu Asn Lys Ala
        675                 680                 685
Phe His Ile Trp Ser Lys Lys Glu Lys Phe Ser Pro Thr Phe Ile Asn
    690                 695                 700
Asn Val Ile Ser His Thr Gly Thr Glu His Ser Ala Pro Ala Trp Met
705                 710                 715                 720
Leu Leu Ser Lys Ile Ala Gly Ser Ser Pro Arg Leu Asp Tyr Ser Arg
                725                 730                 735
Ile Ile Gln Ser Trp Glu Lys Ile Ser Ser Gln Gln Asn Pro Asn Ser
            740                 745                 750
Asn Thr Leu Gly His Ile Leu Cys Val Ile Gly His Ile Ala Lys His
        755                 760                 765
Leu Pro Lys Ser Thr Arg Asp Lys Val Thr Asp Ala Val Lys Cys Lys
    770                 775                 780
Leu Asn Gly Phe Gln Trp Ser Leu Glu Val Ile Ser Ser Ala Val Asp
785                 790                 795                 800
Ala Leu Gln Arg Leu Cys Arg Ala Ser Ala Glu Thr Pro Ala Glu Glu
                805                 810                 815
Gln Glu Leu Leu Thr Gln Val Cys Gly Asp Val Leu Ser Thr Cys Glu
            820                 825                 830
His Arg Leu Ser Asn Ile Val Leu Lys Glu Asn Gly Thr Gly Asn Met
        835                 840                 845
Asp Glu Asp Leu Leu Val Lys Tyr Ile Phe Thr Leu Gly Asp Ile Ala
    850                 855                 860
Gln Leu Cys Pro Ala Arg Val Glu Lys Arg Ile Phe Leu Leu Ile Gln
865                 870                 875                 880
Ser Val Leu Ala Ser Ser Ala Asp Ala Asp His Ser Pro Ser Ser Gln
                885                 890                 895
Gly Ser Ser Glu Ala Pro Ala Ser Gln Pro Pro Pro Gln Val Arg Gly
            900                 905                 910
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Ser Val Met Pro Ser Val Ile Arg Ala His Ala Ile Ile Thr Leu Gly
        915                 920                 925
Lys Leu Cys Leu Gln His Glu Asp Leu Ala Lys Lys Ser Ile Pro Ala
    930                 935                 940
Leu Val Arg Glu Leu Glu Val Cys Glu Asp Val Ala Val Arg Asn Asn
945                 950                 955                 960
Val Ile Ile Val Met Cys Asp Leu Cys Ile Arg Tyr Thr Ile Met Val
                965                 970                 975
Asp Lys Tyr Ile Pro Asn Ile Ser Met Cys Leu Lys Asp Ser Asp Pro
            980                 985                 990
Phe Ile Arg Lys Gln Thr Leu Ile Leu Leu Thr Asn Leu Leu Gln Glu
        995                 1000                1005
Glu Phe Val Lys Trp Lys Gly Ser Leu Phe Phe Arg Phe Val Ser Thr
    1010                1015                1020
Leu Ile Asp Ser His Pro Asp Ile Ala Ser Phe Gly Glu Phe Cys Leu
1025                1030                1035                1040
Ala His Leu Leu Leu Lys Arg Asn Pro Val Met Phe Phe Gln His Phe
                1045                1050                1055
Ile Glu Cys Ile Phe His Phe Asn Asn Tyr Glu Lys His Glu Lys Tyr
            1060                1065                1070
Asn Lys Phe Pro Gln Ser Glu Arg Glu Lys Arg Leu Phe Ser Leu Lys
        1075                1080                1085
Gly Lys Ser Asn Lys Glu Arg Arg Met Lys Ile Tyr Lys Phe Leu Leu
    1090                1095                1100
Glu His Phe Thr Asp Glu Gln Arg Phe Asn Ile Thr Ser Lys Ile Cys
1105                1110                1115                1120
Leu Ser Ile Leu Ala Cys Phe Ala Asp Gly Ile Leu Pro Leu Asp Leu
                1125                1130                1135
Asp Ala Ser Glu Leu Leu Ser Asp Thr Phe Glu Val Leu Ser Ser Lys
            1140                1145                1150
Glu Ile Lys Leu Leu Ala Met Arg Ser Lys Pro Asp Lys Asp Leu Leu
        1155                1160                1165
Met Glu Glu Asp Asp Met Ala Leu Ala Asn Val Val Met Gln Glu Ala
    1170                1175                1180
Gln Lys Lys Leu Ile Ser Gln Val Gln Lys Arg Asn Phe Ile Glu Asn
1185                1190                1195                1200
Ile Ile Pro Ile Ile Ile Ser Leu Lys Thr Val Leu Glu Lys Asn Lys
                1205                1210                1215
Ile Pro Ala Leu Arg Glu Leu Met His Tyr Leu Arg Glu Val Met Gln
            1220                1225                1230
Asp Tyr Arg Asp Glu Leu Lys Asp Phe Phe Ala Val Asp Lys Gln Leu
        1235                1240                1245
Ala Ser Glu Leu Glu Tyr Asp Met Lys Lys Tyr Gln Glu Gln Leu Val
    1250                1255                1260
Gln Glu Gln Glu Leu Ala Lys His Ala Asp Val Ala Gly Thr Ala Gly
1265                1270                1275                1280
Gly Ala Glu Val Ala Pro Val Ala Gln Val Ala Leu Cys Leu Glu Thr
                1285                1290                1295
Val Pro Val Pro Ala Gly Gln Glu Asn Pro Ala Met Ser Pro Ala Val
            1300                1305                1310
Ser Gln Pro Cys Thr Pro Arg Ala Ser Ala Gly His Val Ala Val Ser
        1315                1320                1325
Ser Pro Thr Pro Glu Thr Gly Pro Leu Gln Arg Leu Leu Pro Lys Ala
    1330                1335                1340
Arg Pro Met Ser Leu Ser Thr Ile Ala Ile Leu Asn Ser Val Lys Lys
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1345                1350                1355                1360
Ala Val Glu Ser Lys Ser Arg His Arg Ser Arg Ser Leu Gly Val Leu
                1365                1370                1375
Pro Phe Thr Leu Asn Ser Gly Ser Pro Glu Lys Thr Cys Ser Gln Val
            1380                1385                1390
Ser Ser Tyr Ser Leu Glu Gln Glu Ser Asn Gly Glu Ile Glu His Val
        1395                1400                1405
Thr Lys Arg Ala Ile Ser Thr Pro Glu Lys Ser Ile Ser Asp Val Thr
    1410                1415                1420
Phe Gly Ala Gly Val Ser Tyr Ile Gly Thr Pro Arg Thr Pro Ser Ser
1425                1430                1435                1440
Ala Lys Glu Lys Ile Glu Gly Arg Ser Gln Gly Asn Asp Ile Leu Cys
                1445                1450                1455
Leu Ser Leu Pro Asp Lys Pro Pro Pro Gln Pro Gln Gln Trp Asn Val
            1460                1465                1470
Arg Ser Pro Ala Arg Asn Lys Asp Thr Pro Ala Cys Ser Arg Arg Ser
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Leu Arg Lys Thr Pro Leu Lys Thr Ala Asn
    1490                1495
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gagcacctgt agtcaatcac acgcagcttt taggtttgtt tgaataagag atctgacctg 180
accggcccaa ctgtacaact cttcaaggaa aattcgtatt tgcagtggga agaataagta 240
acattgatca ag atg aat gcc atg ctg gag act ccc gaa ctc cca gcc gtg 291
              Met Asn Ala Met Leu Glu Thr Pro Glu Leu Pro Ala Val
               1               5                  10

ttt gat gga gtg aag ctg gct gca gtg gct gct gtg ctg tac gtg atc   339
Phe Asp Gly Val Lys Leu Ala Ala Val Ala Ala Val Leu Tyr Val Ile
     15                  20                  25

gtc cgg tgt ttg aac ctg aag agc ccc aca gcc cca cct gac ctc tac   387
Val Arg Cys Leu Asn Leu Lys Ser Pro Thr Ala Pro Pro Asp Leu Tyr
 30                  35                  40                  45

ttc cag gac tcg ggg ctc tca cgc ttt ctg ctc aag tcc tgt cct ctt   435
Phe Gln Asp Ser Gly Leu Ser Arg Phe Leu Leu Lys Ser Cys Pro Leu
                 50                  55                  60
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ctg acc aaa gaa tac att cca ccg ttg atc tgg ggg aaa agt gga cac   483
Leu Thr Lys Glu Tyr Ile Pro Pro Leu Ile Trp Gly Lys Ser Gly His
            65                  70                  75

atc cag aca gcc ttg tat ggg aag atg gga agg gtg agg tcg cca cat   531
Ile Gln Thr Ala Leu Tyr Gly Lys Met Gly Arg Val Arg Ser Pro His
        80                  85                  90

cct tat ggg cac cgg aag ttc atc act atg tct gat gga gcc act tct   579
Pro Tyr Gly His Arg Lys Phe Ile Thr Met Ser Asp Gly Ala Thr Ser
    95                  100                 105

aca ttc gac ctc ttc gag ccc ttg gct gag cac tgt gtt gga gat gat   627
Thr Phe Asp Leu Phe Glu Pro Leu Ala Glu His Cys Val Gly Asp Asp
110                 115                 120                 125

atc acc atg gtc atc tgc cct gga att gcc aat cac agc gag aag caa   675
Ile Thr Met Val Ile Cys Pro Gly Ile Ala Asn His Ser Glu Lys Gln
                130                 135                 140

tac atc cgc act ttc gtt gac tac gcc cag aaa aat ggc tat cgg tgc   723
Tyr Ile Arg Thr Phe Val Asp Tyr Ala Gln Lys Asn Gly Tyr Arg Cys
            145                 150                 155

gcc gtg ctg aac cac ctg ggt gcc ctg ccc aac att gaa ttg acc tcg   771
Ala Val Leu Asn His Leu Gly Ala Leu Pro Asn Ile Glu Leu Thr Ser
        160                 165                 170

cca cgc atg ttc acc tat ggc tgc acg tgg gaa ttt gga gcc atg gtg   819
Pro Arg Met Phe Thr Tyr Gly Cys Thr Trp Glu Phe Gly Ala Met Val
    175                 180                 185

aac tac atc aag aag aca tat ccc ctg acc cag ctg gtc gtc gtg ggc   867
Asn Tyr Ile Lys Lys Thr Tyr Pro Leu Thr Gln Leu Val Val Val Gly
190                 195                 200                 205

ttc agc ctg ggt ggt aac att gtg tgc aaa tac ttg ggg gag act cag   915
Phe Ser Leu Gly Gly Asn Ile Val Cys Lys Tyr Leu Gly Glu Thr Gln
                210                 215                 220

gca aac caa gag aag gtc ctg tgc tgc gtc agc gtg tgc cag ggg tac   963
Ala Asn Gln Glu Lys Val Leu Cys Cys Val Ser Val Cys Gln Gly Tyr
            225                 230                 235

agt gca ctg agg gcc cag gaa acc ttc atg caa tgg gat cag tgc cgg   1011
Ser Ala Leu Arg Ala Gln Glu Thr Phe Met Gln Trp Asp Gln Cys Arg
        240                 245                 250

cgg ttc tac aac ttc ctc atg gct gac aac atg aag aag atc atc ctc   1059
Arg Phe Tyr Asn Phe Leu Met Ala Asp Asn Met Lys Lys Ile Ile Leu
    255                 260                 265

tcg cac agg caa gct ctt ttt gga gac cat gtt aag aaa ccc cag agc   1107
Ser His Arg Gln Ala Leu Phe Gly Asp His Val Lys Lys Pro Gln Ser
270                 275                 280                 285
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ctg gaa gac acg gac ttg agc cgg ctc tac aca gca aca tcc ctg atg   1155
Leu Glu Asp Thr Asp Leu Ser Arg Leu Tyr Thr Ala Thr Ser Leu Met
                290                 295                 300

cag att gat gac aat gtg atg agg aag ttt cac ggc tat aac tcc ctg   1203
Gln Ile Asp Asp Asn Val Met Arg Lys Phe His Gly Tyr Asn Ser Leu
            305                 310                 315

aag gaa tac tat gag gaa gaa agt tgc atg cgg tac ctg cac agg att   1251
Lys Glu Tyr Tyr Glu Glu Glu Ser Cys Met Arg Tyr Leu His Arg Ile
        320                 325                 330

tat gtt cct ctc atg ctg gtt aat gca gct gac gat ccg ttg gtg cat   1299
Tyr Val Pro Leu Met Leu Val Asn Ala Ala Asp Asp Pro Leu Val His
    335                 340                 345

gaa agt ctt cta acc att cca aaa tct ctt tca gag aaa cga gag aac   1347
Glu Ser Leu Leu Thr Ile Pro Lys Ser Leu Ser Glu Lys Arg Glu Asn
350                 355                 360                 365

gtc atg ttt gtg ctg cct ctg cat ggg ggc cac ttg ggc ttc ttt gag   1395
Val Met Phe Val Leu Pro Leu His Gly Gly His Leu Gly Phe Phe Glu
                370                 375                 380

ggc tct gtg ctg ttc ccc gag ccc ctg aca tgg atg gat aag ctg gtg   1443
Gly Ser Val Leu Phe Pro Glu Pro Leu Thr Trp Met Asp Lys Leu Val
            385                 390                 395

gtg gag tac gcc aac gcc att tgc caa tgg gag cgt aac aag ttg cag   1491
Val Glu Tyr Ala Asn Ala Ile Cys Gln Trp Glu Arg Asn Lys Leu Gln
        400                 405                 410

tgc tct gac acg gag cag gtg gag gcc gac ctg gag tgaggcctcc        1537
Cys Ser Asp Thr Glu Gln Val Glu Ala Asp Leu Glu
    415                 420                 425

ggactctggc acgctccagc agccctcctc tggaagctgc gtcccctcac cccctgtttc 1597
aggtctccca tctccctcag tgacctggat ctgacctcac accatcagca gggggcaccc 1657
accatgcaca cctgtctcgg agtaggcagc tcttcctggg agctccaggc tatttttgtg 1717
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ccctctgtcc agtttcagca tctggttgct tttaagccaa gtacatctag tttccctatt 1837
aaaaatgtgt ctgaatagcg attttgcttt gccaccaaaa ggcttttccc tgagaacagt 1897
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caccettcca ggccaatgct gaagacacag ctccgcttgg gagcctgaga acccaggctt 2017
cccaggccag agtgtggctt cttaaacggc aaaggraatt cctttgagtc acaagccaag 2077
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tctgggaagg agcctgggga ttttaatttt tcacaagtgc cccagatgat tctcatcacc 2257
aagcaaattt tggaaatgct gttcaacagc gcccttaaat tggaaacatc tttgcagctc 2317
gttttattga aattcataat caggggtgtc ctctagctcc cacggtctcc agagcagcaa 2377
ggccggctat ggagctgccg tcgtgtgacc acagtgtgat gtctcagaag ggctctgggt 2437
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cttcaatttc ttcacctcta aaatggggga cttggaccag gtagattgct gagctcacta 2557
ccaggttcaa agttcaatga caaactcagt ttactgaggt ttgagagaac atccctccag 2617
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gggagcctgg gagctgctct cccagtctaa gcatgtagat atcatcgttt gccttttgtg 2677
tgtgtgtgtc ccttatttga taaaaagatg ttttgagttg ttttttttt taagcactca 2737
cttgtaattt tagtttttaa acccaagtcc ctctaacttt gcctttgata ccaaacaatt 2797
caaaagttgg atctgagttt ggagaaagat atttccaacc taagtgggta ttattttgaa 2857
accagatttt taatttaata gcctatattt gtagtctgtt ggataggtgt ttccaaagtg 2917
tgtcttctca agtgaaaacg caactctagg tttcaagtac tccttttctc cgatcctgtg 2977
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acagaactat gagtaaaatt gcctggatac ttt                              3070

<210> 4
<211> 425
<212> PRT
<213> Homo sapiens

<400> 4
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 1               5                  10                  15
Val Lys Leu Ala Ala Val Ala Ala Val Leu Tyr Val Ile Val Arg Cys
            20                  25                  30
Leu Asn Leu Lys Ser Pro Thr Ala Pro Pro Asp Leu Tyr Phe Gln Asp
        35                  40                  45
Ser Gly Leu Ser Arg Phe Leu Leu Lys Ser Cys Pro Leu Leu Thr Lys
    50                  55                  60
Glu Tyr Ile Pro Pro Leu Ile Trp Gly Lys Ser Gly His Ile Gln Thr
65                  70                  75                  80
Ala Leu Tyr Gly Lys Met Gly Arg Val Arg Ser Pro His Pro Tyr Gly
                85                  90                  95
His Arg Lys Phe Ile Thr Met Ser Asp Gly Ala Thr Ser Thr Phe Asp
            100                 105                 110
Leu Phe Glu Pro Leu Ala Glu His Cys Val Gly Asp Asp Ile Thr Met
        115                 120                 125
Val Ile Cys Pro Gly Ile Ala Asn His Ser Glu Lys Gln Tyr Ile Arg
    130                 135                 140
Thr Phe Val Asp Tyr Ala Gln Lys Asn Gly Tyr Arg Cys Ala Val Leu
145                 150                 155                 160
Asn His Leu Gly Ala Leu Pro Asn Ile Glu Leu Thr Ser Pro Arg Met
                165                 170                 175
Phe Thr Tyr Gly Cys Thr Trp Glu Phe Gly Ala Met Val Asn Tyr Ile
            180                 185                 190
Lys Lys Thr Tyr Pro Leu Thr Gln Leu Val Val Val Gly Phe Ser Leu
        195                 200                 205
Gly Gly Asn Ile Val Cys Lys Tyr Leu Gly Glu Thr Gln Ala Asn Gln
    210                 215                 220
Glu Lys Val Leu Cys Cys Val Ser Val Cys Gln Gly Tyr Ser Ala Leu
225                 230                 235                 240
Arg Ala Gln Glu Thr Phe Met Gln Trp Asp Gln Cys Arg Arg Phe Tyr
                245                 250                 255
Asn Phe Leu Met Ala Asp Asn Met Lys Lys Ile Ile Leu Ser His Arg
            260                 265                 270
Gln Ala Leu Phe Gly Asp His Val Lys Lys Pro Gln Ser Leu Glu Asp
        275                 280                 285
Thr Asp Leu Ser Arg Leu Tyr Thr Ala Thr Ser Leu Met Gln Ile Asp
    290                 295                 300
Asp Asn Val Met Arg Lys Phe His Gly Tyr Asn Ser Leu Lys Glu Tyr
305                 310                 315                 320
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```
Tyr Glu Glu Glu Ser Cys Met Arg Tyr Leu His Arg Ile Tyr Val Pro
                325                 330                 335
Leu Met Leu Val Asn Ala Ala Asp Asp Pro Leu Val His Glu Ser Leu
            340                 345                 350
Leu Thr Ile Pro Lys Ser Leu Ser Glu Lys Arg Glu Asn Val Met Phe
        355                 360                 365
Val Leu Pro Leu His Gly Gly His Leu Gly Phe Phe Glu Gly Ser Val
    370                 375                 380
Leu Phe Pro Glu Pro Leu Thr Trp Met Asp Lys Leu Val Val Glu Tyr
385                 390                 395                 400
Ala Asn Ala Ile Cys Gln Trp Glu Arg Asn Lys Leu Gln Cys Ser Asp
                405                 410                 415
Thr Glu Gln Val Glu Ala Asp Leu Glu
            420                 425
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<210> 5
<211> 2161
<212> DNA
<213> Homo sapiens

<220>
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<222> (138)...(1601)

<221> misc_feature
<222> (0)...(0)
<223> ARP16

<400> 5

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catccccatc ctcgtcgtcg cccggcacag cgcgagcggg cgagcggcgc gggcggccgg 120
agcgccgagg cccggcc atg gcc acc acc agc acc acg ggc tcc acc ctg    170
                    Met Ala Thr Thr Ser Thr Thr Gly Ser Thr Leu
                     1               5                  10

ctg cag ccc ctc agc aac gcc gtg cag ctg ccc atc gac cag gtc aac   218
Leu Gln Pro Leu Ser Asn Ala Val Gln Leu Pro Ile Asp Gln Val Asn
             15                  20                  25

ttt gta gtg tgc caa ctc ttt gcc ttg cta gca gcc att tgg ttt cga   266
Phe Val Val Cys Gln Leu Phe Ala Leu Leu Ala Ala Ile Trp Phe Arg
         30                  35                  40

act tat cta cat tca agc aaa act agc tct ttt ata aga cat gta gtt   314
Thr Tyr Leu His Ser Ser Lys Thr Ser Ser Phe Ile Arg His Val Val
     45                  50                  55

gct acc ctt ttg ggc ctt tat ctt gca ctt ttt tgc ttt gga tgg tat   362
Ala Thr Leu Leu Gly Leu Tyr Leu Ala Leu Phe Cys Phe Gly Trp Tyr
 60                  65                  70                  75

gcc tta cac ttt ctt gta caa agt gga att tcc tac tgt atc atg atc   410
Ala Leu His Phe Leu Val Gln Ser Gly Ile Ser Tyr Cys Ile Met Ile
                 80                  85                  90
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atc ata gga gtg gag aac atg cac aac cca atg atg atc att act cag   458
Ile Ile Gly Val Glu Asn Met His Asn Pro Met Met Ile Ile Thr Gln
             95                  100                 105

aag atc act agt ttg gct tgc gaa att cat gat ggg atg ttt cgg aag   506
Lys Ile Thr Ser Leu Ala Cys Glu Ile His Asp Gly Met Phe Arg Lys
        110                 115                 120

gat gaa gaa ctg act tcc tca cag agg gat tta gct gta agg cgc atg   554
Asp Glu Glu Leu Thr Ser Ser Gln Arg Asp Leu Ala Val Arg Arg Met
    125                 130                 135

cca agc tta ctg gag tat ttg agt tac aac tgt aac ttc atg ggg atc   602
Pro Ser Leu Leu Glu Tyr Leu Ser Tyr Asn Cys Asn Phe Met Gly Ile
140                 145                 150                 155

ctg gca ggc cca ctt tgc tct tac aaa gac tac att act ttc att gaa   650
Leu Ala Gly Pro Leu Cys Ser Tyr Lys Asp Tyr Ile Thr Phe Ile Glu
                160                 165                 170

ggc aga tca tac cat atc aca caa tct ggt gaa aat gga aaa gaa gag   698
Gly Arg Ser Tyr His Ile Thr Gln Ser Gly Glu Asn Gly Lys Glu Glu
            175                 180                 185

aca cag tat gaa aga aca gag cca tct cca aat act gcg gtt gtt cag   746
Thr Gln Tyr Glu Arg Thr Glu Pro Ser Pro Asn Thr Ala Val Val Gln
        190                 195                 200

aag ctc tta gtt tgt ggg ctg tcc ttg tta ttt cac ttg acc atc tgt   794
Lys Leu Leu Val Cys Gly Leu Ser Leu Leu Phe His Leu Thr Ile Cys
    205                 210                 215

aca aca tta cct gtg gag tac aac att gat gag cat ttt caa gct aca   842
Thr Thr Leu Pro Val Glu Tyr Asn Ile Asp Glu His Phe Gln Ala Thr
220                 225                 230                 235

gct tcg tgg cca aca aag att atc tat ctg tat atc tct ctt ttg gct   890
Ala Ser Trp Pro Thr Lys Ile Ile Tyr Leu Tyr Ile Ser Leu Leu Ala
                240                 245                 250

gcc aga ccc aaa tac tat ttt gca tgg acg cta gct gat gcc att aat   938
Ala Arg Pro Lys Tyr Tyr Phe Ala Trp Thr Leu Ala Asp Ala Ile Asn
            255                 260                 265

aat gct gca ggc ttt ggt ttc aga ggg tat gac gaa aat gga gca gct   986
Asn Ala Ala Gly Phe Gly Phe Arg Gly Tyr Asp Glu Asn Gly Ala Ala
        270                 275                 280

cgc tgg gac tta att tcc aat ttg aga att caa caa ata gag atg tca  1034
Arg Trp Asp Leu Ile Ser Asn Leu Arg Ile Gln Gln Ile Glu Met Ser
    285                 290                 295

aca agt ttc aag atg ttt ctt gat aat tgg aat att cag aca gct ctt  1082
Thr Ser Phe Lys Met Phe Leu Asp Asn Trp Asn Ile Gln Thr Ala Leu
```

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300                 305                 310                 315

tgg ctc aaa agg gtg tgt tat gaa cga acc tcc ttc agt cca act atc   1130
Trp Leu Lys Arg Val Cys Tyr Glu Arg Thr Ser Phe Ser Pro Thr Ile
                320                 325                 330

cag acg ttc att ctc tct gcc att tgg cac ggg gta tac cca gga tat   1178
Gln Thr Phe Ile Leu Ser Ala Ile Trp His Gly Val Tyr Pro Gly Tyr
            335                 340                 345

tat cta acg ttt cta aca ggg gtg tta atg aca tta gca gca aga gct   1226
Tyr Leu Thr Phe Leu Thr Gly Val Leu Met Thr Leu Ala Ala Arg Ala
        350                 355                 360

atg aga aat aac ttt aga cat tat ttc att gaa cct tcc caa ctg aaa   1274
Met Arg Asn Asn Phe Arg His Tyr Phe Ile Glu Pro Ser Gln Leu Lys
    365                 370                 375

tta ttt tat gat gtt ata aca tgg ata gta act caa gta gca ata agt   1322
Leu Phe Tyr Asp Val Ile Thr Trp Ile Val Thr Gln Val Ala Ile Ser
380                 385                 390                 395

tac aca gtt gtg cca ttt gtg ctt ctt tct ata aaa cca tca ctc acg   1370
Tyr Thr Val Val Pro Phe Val Leu Leu Ser Ile Lys Pro Ser Leu Thr
                400                 405                 410

ttt tac agc tcc tgg tat tat tgc ctg cac att ctt ggt atc tta gta   1418
Phe Tyr Ser Ser Trp Tyr Tyr Cys Leu His Ile Leu Gly Ile Leu Val
            415                 420                 425

tta ttg ttg ttg cca gtg aaa aaa act caa aga aga aag aat aca cat   1466
Leu Leu Leu Leu Pro Val Lys Lys Thr Gln Arg Arg Lys Asn Thr His
        430                 435                 440

gaa aac att cag ctc tca caa tcc aaa aag ttt gat gaa gga gaa aat   1514
Glu Asn Ile Gln Leu Ser Gln Ser Lys Lys Phe Asp Glu Gly Glu Asn
    445                 450                 455

tct ttg gga cag aac agt ttt tct aca aca aac aat gtt tgc aat cag   1562
Ser Leu Gly Gln Asn Ser Phe Ser Thr Thr Asn Asn Val Cys Asn Gln
460                 465                 470                 475

aat caa gaa ata gcc tcg aga cat tca tca cta aag cag tgatcgggaa    1611
Asn Gln Glu Ile Ala Ser Arg His Ser Ser Leu Lys Gln
                480                 485

ggctctgagg gctgtttttt ttttttgatg ttaacagaaa ccaatcttag caccttttca 1671
aggggtttga gtttgttgga aaagcagtta actgggggga aatggacagt tatagataag 1731
gaatttcctg tacaccagat tggaaatgga gtgaaacaag ccctcccatg ccatgtcccc 1791
gtgggccacg ccttatgtaa gaatatttcc atatttcagt gggcactccc aacctcagca 1851
cttgtccgta gggtcacacg cgtgccctgt tgctgaatgt atgttgcgta tcccaaggca 1911
ctgaagaggt ggaaaaataa tcgtgtcaat ctggatgata gagagaaatt aacttttcca 1971
aatgaatgtc ttgccttaaa ccctctattt cctaaaatat tgttcctaaa tggtattttc 2031
aagtgtaata ttgtgagaac gctactgcag tagttgatgt tgtgtgctgt aaaggatttt 2091
aggaggaatt tgaaacagga tatttaagag tgtggatatt tttaaaatgc aataaacatc 2151
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tcagtatttg 2161

<210> 6
<211> 488
<212> PRT
<213> Homo sapiens

<400> 6

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Met Ala Thr Thr Ser Thr Thr Gly Ser Thr Leu Leu Gln Pro Leu Ser
 1               5                  10                  15
Asn Ala Val Gln Leu Pro Ile Asp Gln Val Asn Phe Val Val Cys Gln
            20                  25                  30
Leu Phe Ala Leu Leu Ala Ala Ile Trp Phe Arg Thr Tyr Leu His Ser
        35                  40                  45
Ser Lys Thr Ser Ser Phe Ile Arg His Val Val Ala Thr Leu Leu Gly
    50                  55                  60
Leu Tyr Leu Ala Leu Phe Cys Phe Gly Trp Tyr Ala Leu His Phe Leu
65                  70                  75                  80
Val Gln Ser Gly Ile Ser Tyr Cys Ile Met Ile Ile Ile Gly Val Glu
                85                  90                  95
Asn Met His Asn Pro Met Met Ile Ile Thr Gln Lys Ile Thr Ser Leu
            100                 105                 110
Ala Cys Glu Ile His Asp Gly Met Phe Arg Lys Asp Glu Glu Leu Thr
        115                 120                 125
Ser Ser Gln Arg Asp Leu Ala Val Arg Arg Met Pro Ser Leu Leu Glu
    130                 135                 140
Tyr Leu Ser Tyr Asn Cys Asn Phe Met Gly Ile Leu Ala Gly Pro Leu
145                 150                 155                 160
Cys Ser Tyr Lys Asp Tyr Ile Thr Phe Ile Glu Gly Arg Ser Tyr His
                165                 170                 175
Ile Thr Gln Ser Gly Glu Asn Gly Lys Glu Glu Thr Gln Tyr Glu Arg
            180                 185                 190
Thr Glu Pro Ser Pro Asn Thr Ala Val Val Gln Lys Leu Leu Val Cys
        195                 200                 205
Gly Leu Ser Leu Leu Phe His Leu Thr Ile Cys Thr Thr Leu Pro Val
    210                 215                 220
Glu Tyr Asn Ile Asp Glu His Phe Gln Ala Thr Ala Ser Trp Pro Thr
225                 230                 235                 240
Lys Ile Ile Tyr Leu Tyr Ile Ser Leu Leu Ala Ala Arg Pro Lys Tyr
                245                 250                 255
Tyr Phe Ala Trp Thr Leu Ala Asp Ala Ile Asn Asn Ala Ala Gly Phe
            260                 265                 270
Gly Phe Arg Gly Tyr Asp Glu Asn Gly Ala Ala Arg Trp Asp Leu Ile
        275                 280                 285
Ser Asn Leu Arg Ile Gln Gln Ile Glu Met Ser Thr Ser Phe Lys Met
    290                 295                 300
Phe Leu Asp Asn Trp Asn Ile Gln Thr Ala Leu Trp Leu Lys Arg Val
305                 310                 315                 320
Cys Tyr Glu Arg Thr Ser Phe Ser Pro Thr Ile Gln Thr Phe Ile Leu
                325                 330                 335
Ser Ala Ile Trp His Gly Val Tyr Pro Gly Tyr Tyr Leu Thr Phe Leu
            340                 345                 350
Thr Gly Val Leu Met Thr Leu Ala Ala Arg Ala Met Arg Asn Asn Phe
        355                 360                 365
Arg His Tyr Phe Ile Glu Pro Ser Gln Leu Lys Leu Phe Tyr Asp Val
```

```
    370                 375                 380
Ile Thr Trp Ile Val Thr Gln Val Ala Ile Ser Tyr Thr Val Val Pro
385                 390                 395                 400
Phe Val Leu Leu Ser Ile Lys Pro Ser Leu Thr Phe Tyr Ser Ser Trp
                405                 410                 415
Tyr Tyr Cys Leu His Ile Leu Gly Ile Leu Val Leu Leu Leu Leu Pro
            420                 425                 430
Val Lys Lys Thr Gln Arg Arg Lys Asn Thr His Glu Asn Ile Gln Leu
        435                 440                 445
Ser Gln Ser Lys Lys Phe Asp Glu Gly Glu Asn Ser Leu Gly Gln Asn
    450                 455                 460
Ser Phe Ser Thr Thr Asn Asn Val Cys Asn Gln Asn Gln Glu Ile Ala
465                 470                 475                 480
Ser Arg His Ser Ser Leu Lys Gln
                485
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<210> 7
<211> 2096
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)...(1728)

<221> misc_feature
<222> (0)...(0)
<223> ARP8

<400> 7

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agc ggg gac ctc cag gat tac cgc tgc tcc agg gac tca gcc ccg agc   48
Ser Gly Asp Leu Gln Asp Tyr Arg Cys Ser Arg Asp Ser Ala Pro Ser
 1               5                  10                  15

ccc gtg ccc cat gag ctg gtg atc acc atc gaa ctg ccg ctg ttg cgc   96
Pro Val Pro His Glu Leu Val Ile Thr Ile Glu Leu Pro Leu Leu Arg
            20                  25                  30

tcg gcc gag cag gcg gcg ctg gag gta acg aga aag ctg ctg tgc ctc   144
Ser Ala Glu Gln Ala Ala Leu Glu Val Thr Arg Lys Leu Leu Cys Leu
        35                  40                  45

gac tcg agg aaa cct gac tac cgg ctg cgg ctc tcg ctc ccg tac cca   192
Asp Ser Arg Lys Pro Asp Tyr Arg Leu Arg Leu Ser Leu Pro Tyr Pro
    50                  55                  60

gtg gac gat ggc cgc ggc aag gca caa ttc aac aag gcc cgg cgg cag   240
Val Asp Asp Gly Arg Gly Lys Ala Gln Phe Asn Lys Ala Arg Arg Gln
65                  70                  75                  80

ctg gtg gtt acg ctg cca gtg gtg ctg ccg gcc gcg cgc cgg gag ccc   288
Leu Val Val Thr Leu Pro Val Val Leu Pro Ala Ala Arg Arg Glu Pro
                85                  90                  95
```

```
gct gtc gcc gtc gcc gcc gcc gcg ccg gaa gag tcc gcg gac cgg tcc   336
Ala Val Ala Val Ala Ala Ala Ala Pro Glu Glu Ser Ala Asp Arg Ser
            100                 105                 110

gga act gac ggc cag gcc tgc gct tcc gct cgc gag ggg gag gcg gga   384
Gly Thr Asp Gly Gln Ala Cys Ala Ser Ala Arg Glu Gly Glu Ala Gly
        115                 120                 125

ccc gcg agg agt cgc gcc gag gac gga ggc cac gat acc tgc gtg gct   432
Pro Ala Arg Ser Arg Ala Glu Asp Gly Gly His Asp Thr Cys Val Ala
    130                 135                 140

ggg gct gcg ggc tcc ggg gtc acc acc ctg ggc gac ccg gag gtg gcg   480
Gly Ala Ala Gly Ser Gly Val Thr Thr Leu Gly Asp Pro Glu Val Ala
145                 150                 155                 160

cct ccg ccg gcc gca gct gga gag gag cgt gtc ccc aag ccg ggg gag   528
Pro Pro Pro Ala Ala Ala Gly Glu Glu Arg Val Pro Lys Pro Gly Glu
                165                 170                 175

cag gac ttg agc agg cac gcg ggg tca ccg ccg ggc agc gtg gag gag   576
Gln Asp Leu Ser Arg His Ala Gly Ser Pro Pro Gly Ser Val Glu Glu
            180                 185                 190

cca tct cct gga gga gaa aac tca cct ggt ggc gga ggc tcc cct tgt   624
Pro Ser Pro Gly Gly Glu Asn Ser Pro Gly Gly Gly Gly Ser Pro Cys
        195                 200                 205

ttg tcc tcc cgg agc ctg gcg tgg ggt tct tct gcg gga aga gag agt   672
Leu Ser Ser Arg Ser Leu Ala Trp Gly Ser Ser Ala Gly Arg Glu Ser
    210                 215                 220

gcg cgc gga gat agc agt gtg gaa acg cgc gag gag tcg gag ggc acg   720
Ala Arg Gly Asp Ser Ser Val Glu Thr Arg Glu Glu Ser Glu Gly Thr
225                 230                 235                 240

ggc ggc cag cgc tca gcc tgc gcc atg ggt ggt ccc ggg acc aag agc   768
Gly Gly Gln Arg Ser Ala Cys Ala Met Gly Gly Pro Gly Thr Lys Ser
                245                 250                 255

ggg gag cct ttg tgt cct ccg tta ctg tgt aat cag gac aaa gaa acc   816
Gly Glu Pro Leu Cys Pro Pro Leu Leu Cys Asn Gln Asp Lys Glu Thr
            260                 265                 270

ttg act ctg ctc att cag gtg cct cgg atc cag ccg caa agt ctt caa   864
Leu Thr Leu Leu Ile Gln Val Pro Arg Ile Gln Pro Gln Ser Leu Gln
        275                 280                 285

gga gat ttg aat ccc ctc tgg tac aaa tta cgc ttc tcc gca caa gac   912
Gly Asp Leu Asn Pro Leu Trp Tyr Lys Leu Arg Phe Ser Ala Gln Asp
    290                 295                 300

tta gtt tat tcc ttc ttt ttg caa ttt gct cca gag aat aaa ttg agt   960
Leu Val Tyr Ser Phe Phe Leu Gln Phe Ala Pro Glu Asn Lys Leu Ser
305                 310                 315                 320
```

```
acc aca gaa cct gtg att agc att tct tca aac aat gca gtg ata gaa   1008
Thr Thr Glu Pro Val Ile Ser Ile Ser Ser Asn Asn Ala Val Ile Glu
                325                 330                 335

ctg gca aaa tct cca gag agc cat gga cat tgg aga gag tgg tat tat   1056
Leu Ala Lys Ser Pro Glu Ser His Gly His Trp Arg Glu Trp Tyr Tyr
            340                 345                 350

ggt gta aac aac gat tct ttg gag gaa agg tta ttt gtc aat gaa gaa   1104
Gly Val Asn Asn Asp Ser Leu Glu Glu Arg Leu Phe Val Asn Glu Glu
        355                 360                 365

aat gtt aat gag ttt ctt gaa gag gtc ctg agc tct cca ttc aaa cag   1152
Asn Val Asn Glu Phe Leu Glu Glu Val Leu Ser Ser Pro Phe Lys Gln
    370                 375                 380

tct atg tcc ttg acc cca cca tta att gaa gtt ctt caa gtt act gat   1200
Ser Met Ser Leu Thr Pro Pro Leu Ile Glu Val Leu Gln Val Thr Asp
385                 390                 395                 400

aat aag att caa att aat gca aag ttg caa gaa tgt agt aac tct gat   1248
Asn Lys Ile Gln Ile Asn Ala Lys Leu Gln Glu Cys Ser Asn Ser Asp
                405                 410                 415

cag cta caa gga aag gag gaa aga gta aat gaa gaa agt cat cta act   1296
Gln Leu Gln Gly Lys Glu Glu Arg Val Asn Glu Glu Ser His Leu Thr
            420                 425                 430

gaa aag gaa tat ata gaa cat tgt aac acc cct aca act gat tct gat   1344
Glu Lys Glu Tyr Ile Glu His Cys Asn Thr Pro Thr Thr Asp Ser Asp
        435                 440                 445

tca tct ata gca gtt aaa gca cta caa ata gat agc ttt ggt tta gtt   1392
Ser Ser Ile Ala Val Lys Ala Leu Gln Ile Asp Ser Phe Gly Leu Val
    450                 455                 460

aca tgc ttt caa caa gag tct ctt gat gtt tct caa atg ata ctt gga   1440
Thr Cys Phe Gln Gln Glu Ser Leu Asp Val Ser Gln Met Ile Leu Gly
465                 470                 475                 480

aaa tct cag caa cct gag tca aaa atg caa tct gaa ttt ata aaa gaa   1488
Lys Ser Gln Gln Pro Glu Ser Lys Met Gln Ser Glu Phe Ile Lys Glu
                485                 490                 495

aaa agt gct act tgt tca aat gag gaa aaa gat aac tta aac gag tca   1536
Lys Ser Ala Thr Cys Ser Asn Glu Glu Lys Asp Asn Leu Asn Glu Ser
            500                 505                 510

gta ata act gaa gag aaa gaa aca gat gga gat cac cta tct tca tta   1584
Val Ile Thr Glu Glu Lys Glu Thr Asp Gly Asp His Leu Ser Ser Leu
        515                 520                 525

ctg aac aaa act acg gtt cac aat ata cct gga ttc gac agc ata aaa   1632
Leu Asn Lys Thr Thr Val His Asn Ile Pro Gly Phe Asp Ser Ile Lys
```

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    530                 535                 540

gaa acc aat atg cag gat ggt agt gtg cag gtc att aaa gat cat gtg   1680
Glu Thr Asn Met Gln Asp Gly Ser Val Gln Val Ile Lys Asp His Val
545                 550                 555                 560

acc aat tgt gca ttc agt ttt cag aat tct ttg cta tat gat ttg gat   1728
Thr Asn Cys Ala Phe Ser Phe Gln Asn Ser Leu Leu Tyr Asp Leu Asp
                565                 570                 575

taattctata taattttgga cttttaaata ttaaggttaa aaaatacctg tatctaaaat 1788
tgattctgtt aactgttgtc ttaaaactaa aggtattaaa gtataaaatt aaaatttgca 1848
attttttta aaaaattgca attttgattc tcatggggga aattggagat aatttttttt 1908
ttttgcctct ggagtttaaa gtttccttat ggagataagt tttgtgattc ctgtaataga 1968
tgtgtatgtt ttctatttga gagttaaaac atttgagagt taaaacattt agttttaata 2028
caacctatgt atatatactt ctgtgttaaa ttttgctttg tcattaataa aatttaaaaa 2088
tattcact                                                          2096

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<212> PRT
<213> Homo sapiens

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            20                  25                  30
Ser Ala Glu Gln Ala Ala Leu Glu Val Thr Arg Lys Leu Leu Cys Leu
        35                  40                  45
Asp Ser Arg Lys Pro Asp Tyr Arg Leu Arg Leu Ser Leu Pro Tyr Pro
    50                  55                  60
Val Asp Asp Gly Arg Gly Lys Ala Gln Phe Asn Lys Ala Arg Arg Gln
65                  70                  75                  80
Leu Val Val Thr Leu Pro Val Val Leu Pro Ala Ala Arg Arg Glu Pro
                85                  90                  95
Ala Val Ala Val Ala Ala Ala Ala Pro Glu Glu Ser Ala Asp Arg Ser
            100                 105                 110
Gly Thr Asp Gly Gln Ala Cys Ala Ser Ala Arg Glu Gly Glu Ala Gly
        115                 120                 125
Pro Ala Arg Ser Arg Ala Glu Asp Gly Gly His Asp Thr Cys Val Ala
    130                 135                 140
Gly Ala Ala Gly Ser Gly Val Thr Thr Leu Gly Asp Pro Glu Val Ala
145                 150                 155                 160
Pro Pro Pro Ala Ala Ala Gly Glu Glu Arg Val Pro Lys Pro Gly Glu
                165                 170                 175
Gln Asp Leu Ser Arg His Ala Gly Ser Pro Pro Gly Ser Val Glu Glu
            180                 185                 190
Pro Ser Pro Gly Gly Glu Asn Ser Pro Gly Gly Gly Gly Ser Pro Cys
        195                 200                 205
Leu Ser Ser Arg Ser Leu Ala Trp Gly Ser Ser Ala Gly Arg Glu Ser
    210                 215                 220
Ala Arg Gly Asp Ser Ser Val Glu Thr Arg Glu Glu Ser Glu Gly Thr
225                 230                 235                 240
Gly Gly Gln Arg Ser Ala Cys Ala Met Gly Gly Pro Gly Thr Lys Ser
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                245                 250                 255
Gly Glu Pro Leu Cys Pro Pro Leu Leu Cys Asn Gln Asp Lys Glu Thr
            260                 265                 270
Leu Thr Leu Leu Ile Gln Val Pro Arg Ile Gln Pro Gln Ser Leu Gln
        275                 280                 285
Gly Asp Leu Asn Pro Leu Trp Tyr Lys Leu Arg Phe Ser Ala Gln Asp
    290                 295                 300
Leu Val Tyr Ser Phe Phe Leu Gln Phe Ala Pro Glu Asn Lys Leu Ser
305                 310                 315                 320
Thr Thr Glu Pro Val Ile Ser Ile Ser Ser Asn Asn Ala Val Ile Glu
                325                 330                 335
Leu Ala Lys Ser Pro Glu Ser His Gly His Trp Arg Glu Trp Tyr Tyr
            340                 345                 350
Gly Val Asn Asn Asp Ser Leu Glu Glu Arg Leu Phe Val Asn Glu Glu
        355                 360                 365
Asn Val Asn Glu Phe Leu Glu Glu Val Leu Ser Ser Pro Phe Lys Gln
    370                 375                 380
Ser Met Ser Leu Thr Pro Pro Leu Ile Glu Val Leu Gln Val Thr Asp
385                 390                 395                 400
Asn Lys Ile Gln Ile Asn Ala Lys Leu Gln Glu Cys Ser Asn Ser Asp
                405                 410                 415
Gln Leu Gln Gly Lys Glu Glu Arg Val Asn Glu Glu Ser His Leu Thr
            420                 425                 430
Glu Lys Glu Tyr Ile Glu His Cys Asn Thr Pro Thr Thr Asp Ser Asp
        435                 440                 445
Ser Ser Ile Ala Val Lys Ala Leu Gln Ile Asp Ser Phe Gly Leu Val
    450                 455                 460
Thr Cys Phe Gln Gln Glu Ser Leu Asp Val Ser Gln Met Ile Leu Gly
465                 470                 475                 480
Lys Ser Gln Gln Pro Glu Ser Lys Met Gln Ser Glu Phe Ile Lys Glu
                485                 490                 495
Lys Ser Ala Thr Cys Ser Asn Glu Glu Lys Asp Asn Leu Asn Glu Ser
            500                 505                 510
Val Ile Thr Glu Glu Lys Glu Thr Asp Gly Asp His Leu Ser Ser Leu
        515                 520                 525
Leu Asn Lys Thr Thr Val His Asn Ile Pro Gly Phe Asp Ser Ile Lys
    530                 535                 540
Glu Thr Asn Met Gln Asp Gly Ser Val Gln Val Ile Lys Asp His Val
545                 550                 555                 560
Thr Asn Cys Ala Phe Ser Phe Gln Asn Ser Leu Leu Tyr Asp Leu Asp
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<223> ARP9

<400> 9

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ccgccgccgc cgccgccgca ccacgttccc cacccggggc tgcgtcaccg ggagacacgt 180
tcccagccag catgggtcgg cgcccagcgg cccgcccgag cactccggcc gcagaaccag 240
agtgccgccc tgaggcctgc tgagaacaca acaccctccc gaccgcgcca ccgcgccccc 300
ctagccgggc gcgtccttgc agggcctggg ctgtctccct cccactctca gaaataaggc 360
acacgcctgg gcattcgtgg gccaacgggc cttggctaaa ccgtccccac atttgtcagc 420
gccacagcaa catcctcaga gtctgagcga actgcgccca gcgcgggcac ggagcctccc 480
accgccagca acctgcggcc ccggagaagg cagcgagcgc agtgacagcg cctcaccgcc 540
accagctcct ggaccacc atg gcc aag aac cgc agg gac aga aac agt tgg   591
                    Met Ala Lys Asn Arg Arg Asp Arg Asn Ser Trp
                     1               5                  10

ggt gga ttt tcg gaa aag aca tat gaa tgg agc tca gaa gag gag gag   639
Gly Gly Phe Ser Glu Lys Thr Tyr Glu Trp Ser Ser Glu Glu Glu Glu
            15                  20                  25

cca gtg aaa aag gca gga cca gtc caa gtc ctc att gtc aaa gat gac   687
Pro Val Lys Lys Ala Gly Pro Val Gln Val Leu Ile Val Lys Asp Asp
        30                  35                  40

cat tcc ttt gag tta gat gaa act gca tta aat cgg atc ctt ctc tcg   735
His Ser Phe Glu Leu Asp Glu Thr Ala Leu Asn Arg Ile Leu Leu Ser
    45                  50                  55

gag gct gtc aga gac aag gag gtt gtt gct gta tct gtt gct gga gca   783
Glu Ala Val Arg Asp Lys Glu Val Val Ala Val Ser Val Ala Gly Ala
60                  65                  70                  75

ttt aga aaa gga aaa tca ttc ctg atg gac ttc atg ttg aga tac atg   831
Phe Arg Lys Gly Lys Ser Phe Leu Met Asp Phe Met Leu Arg Tyr Met
                80                  85                  90

tac aac cag gaa tca gtt gat tgg gtt gga gac tac aat gaa cca ttg   879
Tyr Asn Gln Glu Ser Val Asp Trp Val Gly Asp Tyr Asn Glu Pro Leu
            95                  100                 105

act ggt ttt tca tgg aga ggt gga tct gaa cga gag acc aca gga att   927
Thr Gly Phe Ser Trp Arg Gly Gly Ser Glu Arg Glu Thr Thr Gly Ile
        110                 115                 120

cag ata tgg agt gaa atc ttc ctt atc aat aaa cct gat ggt aaa aag   975
Gln Ile Trp Ser Glu Ile Phe Leu Ile Asn Lys Pro Asp Gly Lys Lys
    125                 130                 135

gtt gca gtg tta ttg atg gat act cag gga acc ttt gat agt cag tca   1023
Val Ala Val Leu Leu Met Asp Thr Gln Gly Thr Phe Asp Ser Gln Ser
140                 145                 150                 155

act ttg aga gat tca gcc aca gta ttt gcc ctt agc aca atg atc agc   1071
Thr Leu Arg Asp Ser Ala Thr Val Phe Ala Leu Ser Thr Met Ile Ser
                160                 165                 170
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tca ata cag gta tat aac tta tcc caa aat gtc cag gag gat gat ctt   1119
Ser Ile Gln Val Tyr Asn Leu Ser Gln Asn Val Gln Glu Asp Asp Leu
            175                 180                 185

cag cac ctc cag ctt ttc act gag tat ggc aga ctg gca atg gag gaa   1167
Gln His Leu Gln Leu Phe Thr Glu Tyr Gly Arg Leu Ala Met Glu Glu
        190                 195                 200

aca ttc ctg aag cca ttt cag agt ctg ata ttt ctt gtt cga gac tgg   1215
Thr Phe Leu Lys Pro Phe Gln Ser Leu Ile Phe Leu Val Arg Asp Trp
    205                 210                 215

agt ttc cca tac gaa ttt tca tat gga gcc gat ggt ggt gcc aaa ttc   1263
Ser Phe Pro Tyr Glu Phe Ser Tyr Gly Ala Asp Gly Gly Ala Lys Phe
220                 225                 230                 235

ttg gaa aaa cgc ctc aag gtc tca ggg aac cag cat gaa gaa cta cag   1311
Leu Glu Lys Arg Leu Lys Val Ser Gly Asn Gln His Glu Glu Leu Gln
                240                 245                 250

aac gtc aga aaa cac atc cat tcc tgt ttc acc aac att tcc tgt ttt   1359
Asn Val Arg Lys His Ile His Ser Cys Phe Thr Asn Ile Ser Cys Phe
            255                 260                 265

ctg cta cct cat cct ggc tta aaa gta gct acc aat cca aac ttt gat   1407
Leu Leu Pro His Pro Gly Leu Lys Val Ala Thr Asn Pro Asn Phe Asp
        270                 275                 280

gga aaa ttg aaa gaa ata gat gat gaa ttc atc aaa aac ttg aaa ata   1455
Gly Lys Leu Lys Glu Ile Asp Asp Glu Phe Ile Lys Asn Leu Lys Ile
    285                 290                 295

ctg att cct tgg cta ctt agt ccc gag agc cta gat att aaa gag atc   1503
Leu Ile Pro Trp Leu Leu Ser Pro Glu Ser Leu Asp Ile Lys Glu Ile
300                 305                 310                 315

aat ggg aat aaa atc acc tgc cgg ggt ctg gtg gag tac ttc aag gct   1551
Asn Gly Asn Lys Ile Thr Cys Arg Gly Leu Val Glu Tyr Phe Lys Ala
                320                 325                 330

tat ata aag atc tat caa ggt gaa gaa tta cca cat ccc aaa tcc atg   1599
Tyr Ile Lys Ile Tyr Gln Gly Glu Glu Leu Pro His Pro Lys Ser Met
            335                 340                 345

tta cag gcc aca gca gaa gct aac aat tta gca gcc gtg gca act gcc   1647
Leu Gln Ala Thr Ala Glu Ala Asn Asn Leu Ala Ala Val Ala Thr Ala
        350                 355                 360

aag gac aca tac aac aaa aaa atg gaa gag att tgt ggt ggt gac aaa   1695
Lys Asp Thr Tyr Asn Lys Lys Met Glu Glu Ile Cys Gly Gly Asp Lys
    365                 370                 375

cca ttt ctg gcc cca aat gac ttg cag acc aaa cac ctg caa ctt aag   1743
Pro Phe Leu Ala Pro Asn Asp Leu Gln Thr Lys His Leu Gln Leu Lys
380                 385                 390                 395
```

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gaa gaa tct gtg aag cta ttc cga ggg gtg aag aag atg ggt ggg gaa   1791
Glu Glu Ser Val Lys Leu Phe Arg Gly Val Lys Lys Met Gly Gly Glu
                400                 405                 410

gaa ttt agc cgg cgt tac ctg cag cag ttg gag agt gaa ata gat gaa   1839
Glu Phe Ser Arg Arg Tyr Leu Gln Gln Leu Glu Ser Glu Ile Asp Glu
            415                 420                 425

ctt tac atc caa tat atc aag cac aat gat agc aaa aat atc ttc cat   1887
Leu Tyr Ile Gln Tyr Ile Lys His Asn Asp Ser Lys Asn Ile Phe His
        430                 435                 440

gca gct cgt acc cca gcc aca ctg ttt gta gtc atc ttt atc aca tat   1935
Ala Ala Arg Thr Pro Ala Thr Leu Phe Val Val Ile Phe Ile Thr Tyr
    445                 450                 455

gtg att gct ggt gtg act gga ttc att ggt ttg gac atc ata gct agc   1983
Val Ile Ala Gly Val Thr Gly Phe Ile Gly Leu Asp Ile Ile Ala Ser
460                 465                 470                 475

cta tgc aat atg ata atg gga ctg acc ctt atc acc ctg tgc act tgg   2031
Leu Cys Asn Met Ile Met Gly Leu Thr Leu Ile Thr Leu Cys Thr Trp
                480                 485                 490

gca tat atc cgg tac tct gga gaa tac cga gag ctg gga gct gta ata   2079
Ala Tyr Ile Arg Tyr Ser Gly Glu Tyr Arg Glu Leu Gly Ala Val Ile
            495                 500                 505

gac cag gtg gct gca gct ctg tgg gac cag gga agt aca aat gag gct   2127
Asp Gln Val Ala Ala Ala Leu Trp Asp Gln Gly Ser Thr Asn Glu Ala
        510                 515                 520

ttg tac aag ctt tac agt gca gca gca acc cac aga cat ctg tat cat   2175
Leu Tyr Lys Leu Tyr Ser Ala Ala Ala Thr His Arg His Leu Tyr His
    525                 530                 535

caa gct ttc cct aca cca aag tcg gaa tct act gaa caa tca gaa aag   2223
Gln Ala Phe Pro Thr Pro Lys Ser Glu Ser Thr Glu Gln Ser Glu Lys
540                 545                 550                 555

aaa aaa atg taatgcaaat tttaagaaat acaggtgcat gaccaattgt           2272
Lys Lys Met
```

```
caattaaata ttcagtttta tgtctccatg caaacattca aagtgcttcc atcagaacgg 2332
agtaaaatac taaacacctc tgaagactgc aaactggatt agttctttta cttcagtgtt 2392
taataagcag atgtatgtat gcatggttat actattttgt taacatgtac aatttcctga 2452
tttttcttca aaaatgctgt tataaagtat ttgtctattt atgataacag tacacgtgtt 2512
ctgcttgaat ttactaaatt ctactactgg gttataatta aatcatgtga tattcc     2568
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<210> 10
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<212> PRT
<213> Homo sapiens

<400> 10

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 1               5                  10                  15
Lys Thr Tyr Glu Trp Ser Ser Glu Glu Glu Glu Pro Val Lys Lys Ala
            20                  25                  30
Gly Pro Val Gln Val Leu Ile Val Lys Asp Asp His Ser Phe Glu Leu
        35                  40                  45
Asp Glu Thr Ala Leu Asn Arg Ile Leu Leu Ser Glu Ala Val Arg Asp
    50                  55                  60
Lys Glu Val Val Ala Val Ser Val Ala Gly Ala Phe Arg Lys Gly Lys
65                  70                  75                  80
Ser Phe Leu Met Asp Phe Met Leu Arg Tyr Met Tyr Asn Gln Glu Ser
                85                  90                  95
Val Asp Trp Val Gly Asp Tyr Asn Glu Pro Leu Thr Gly Phe Ser Trp
            100                 105                 110
Arg Gly Gly Ser Glu Arg Glu Thr Thr Gly Ile Gln Ile Trp Ser Glu
        115                 120                 125
Ile Phe Leu Ile Asn Lys Pro Asp Gly Lys Lys Val Ala Val Leu Leu
    130                 135                 140
Met Asp Thr Gln Gly Thr Phe Asp Ser Gln Ser Thr Leu Arg Asp Ser
145                 150                 155                 160
Ala Thr Val Phe Ala Leu Ser Thr Met Ile Ser Ser Ile Gln Val Tyr
                165                 170                 175
Asn Leu Ser Gln Asn Val Gln Glu Asp Asp Leu Gln His Leu Gln Leu
            180                 185                 190
Phe Thr Glu Tyr Gly Arg Leu Ala Met Glu Glu Thr Phe Leu Lys Pro
        195                 200                 205
Phe Gln Ser Leu Ile Phe Leu Val Arg Asp Trp Ser Phe Pro Tyr Glu
    210                 215                 220
Phe Ser Tyr Gly Ala Asp Gly Gly Ala Lys Phe Leu Glu Lys Arg Leu
225                 230                 235                 240
Lys Val Ser Gly Asn Gln His Glu Glu Leu Gln Asn Val Arg Lys His
                245                 250                 255
Ile His Ser Cys Phe Thr Asn Ile Ser Cys Phe Leu Leu Pro His Pro
            260                 265                 270
Gly Leu Lys Val Ala Thr Asn Pro Asn Phe Asp Gly Lys Leu Lys Glu
        275                 280                 285
Ile Asp Asp Glu Phe Ile Lys Asn Leu Lys Ile Leu Ile Pro Trp Leu
    290                 295                 300
Leu Ser Pro Glu Ser Leu Asp Ile Lys Glu Ile Asn Gly Asn Lys Ile
305                 310                 315                 320
Thr Cys Arg Gly Leu Val Glu Tyr Phe Lys Ala Tyr Ile Lys Ile Tyr
                325                 330                 335
Gln Gly Glu Glu Leu Pro His Pro Lys Ser Met Leu Gln Ala Thr Ala
            340                 345                 350
Glu Ala Asn Asn Leu Ala Ala Val Ala Thr Ala Lys Asp Thr Tyr Asn
        355                 360                 365
Lys Lys Met Glu Glu Ile Cys Gly Gly Asp Lys Pro Phe Leu Ala Pro
    370                 375                 380
Asn Asp Leu Gln Thr Lys His Leu Gln Leu Lys Glu Glu Ser Val Lys
385                 390                 395                 400
Leu Phe Arg Gly Val Lys Lys Met Gly Gly Glu Glu Phe Ser Arg Arg
                405                 410                 415
Tyr Leu Gln Gln Leu Glu Ser Glu Ile Asp Glu Leu Tyr Ile Gln Tyr
```

```
            420                 425                 430
Ile Lys His Asn Asp Ser Lys Asn Ile Phe His Ala Ala Arg Thr Pro
        435                 440                 445
Ala Thr Leu Phe Val Val Ile Phe Ile Thr Tyr Val Ile Ala Gly Val
    450                 455                 460
Thr Gly Phe Ile Gly Leu Asp Ile Ile Ala Ser Leu Cys Asn Met Ile
465                 470                 475                 480
Met Gly Leu Thr Leu Ile Thr Leu Cys Thr Trp Ala Tyr Ile Arg Tyr
                485                 490                 495
Ser Gly Glu Tyr Arg Glu Leu Gly Ala Val Ile Asp Gln Val Ala Ala
            500                 505                 510
Ala Leu Trp Asp Gln Gly Ser Thr Asn Glu Ala Leu Tyr Lys Leu Tyr
        515                 520                 525
Ser Ala Ala Ala Thr His Arg His Leu Tyr His Gln Ala Phe Pro Thr
    530                 535                 540
Pro Lys Ser Glu Ser Thr Glu Gln Ser Glu Lys Lys Lys Met
545                 550                 555
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<211> 2920
<212> DNA
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agaggccctc ggtggtgccc atg gct ggc cag gat cct gcg ctg agc acg agt 173
                      Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser
                       1               5                  10

cac ccg ttc tac gac gtg gcc aga cat ggc att ctg cag gtg gca ggg   221
His Pro Phe Tyr Asp Val Ala Arg His Gly Ile Leu Gln Val Ala Gly
            15                  20                  25

gat gac cgc ttt gga aga cgt gtt gtc acg ttc agc tgc tgc cgg atg   269
Asp Asp Arg Phe Gly Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met
        30                  35                  40

cca ccc tcc cac gag ctg gac cac cag cgg ctg ctg gag tat ttg aag   317
Pro Pro Ser His Glu Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys
    45                  50                  55

tac aca ctg gac caa tac gtt gag aac gat tat acc atc gtc tat ttc   365
Tyr Thr Leu Asp Gln Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe
60                  65                  70                  75
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cac tac ggg ctg aac agc cgg aac aag cct tcc ctg ggc tgg ctc cag   413
His Tyr Gly Leu Asn Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu Gln
                 80                  85                  90

agc gca tac aag gag ttc gat agg aag tac aag aag aac ttg aag gcc   461
Ser Ala Tyr Lys Glu Phe Asp Arg Lys Tyr Lys Lys Asn Leu Lys Ala
            95                 100                 105

ctc tac gtg gtg cac ccc acc agc ttc atc aag gtc ctg tgg aac atc   509
Leu Tyr Val Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile
        110                 115                 120

ttg aag ccc ctc atc agt cac aag ttt ggg aag aaa gtc atc tat ttc   557
Leu Lys Pro Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe
    125                 130                 135

aac tac ctg agt gag ctc cac gaa cac ctt aaa tac gac cag ctg gtc   605
Asn Tyr Leu Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val
140                 145                 150                 155

atc cct ccc gaa gtt ttg cgg tac gat gag aag ctc cag agc ctg cac   653
Ile Pro Pro Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His
                160                 165                 170

gag ggc cgg acg ccg cct ccc acc aag aca cca ccg ccg cgg ccc ccg   701
Glu Gly Arg Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro
            175                 180                 185

ctg ccc aca cag cag ttt ggc gtc agt ctg caa tac ctc aaa gac aaa   749
Leu Pro Thr Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys
        190                 195                 200

aat caa ggc gaa ctc atc ccc cct gtg ctg agg ttc aca gtg acg tac   797
Asn Gln Gly Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr
    205                 210                 215

ctg aga gag aaa ggc ctg cgc acc gag ggc ctg ttc cgg aga tcc gcc   845
Leu Arg Glu Lys Gly Leu Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala
220                 225                 230                 235

agc gtg cag acc gtc cgc gag atc cag agg ctc tac aac caa ggg aag   893
Ser Val Gln Thr Val Arg Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys
                240                 245                 250

ccc gtg aac ttt gac gac tac ggg gac att cac atc cct gcc gtg atc   941
Pro Val Asn Phe Asp Asp Tyr Gly Asp Ile His Ile Pro Ala Val Ile
            255                 260                 265

ctg aag acc ttc ctg cga gag ctg ccc cag ccg ctt ctg acc ttc cag   989
Leu Lys Thr Phe Leu Arg Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln
        270                 275                 280

gcc tac gag cag att ctc ggg atc acc tgt gcg tagctgccct ggcgcagggg 1042
Ala Tyr Glu Gln Ile Leu Gly Ile Thr Cys Ala
    285                 290
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tgggggggctt ggtcctcaga tgctgtcccc cagctactgg cccagggtca ggctctgggg 1102
tggccgaggt gacgtgtacc caccctcctc ctgttgccat ctggcactgc agggcaagag 1162
agggggttgt tggggctgcc cccaccatgc acagccagtc cacactgtcc aaaggcagag 1222
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ttggtgtgaa ttctgaagca gctcggttaa gatatcgtaa agacaaatct tgaatcttaa 1762
aatcaatgtt tctaccccac tgtgtattca agaatcacat ttgcccaaag ggcagcctgg 1822
cctttgtcct ggcccctggg gggtgacttc tgaaccttgc actttcccaa ggggcaggag 1882
ttacctttgt cactcatcag gggccctgat ggtttatggt aactcatggt tatggtgtga 1942
ctcaagatag gggtgtaggg gtggccattc cagaaagacc aattacatgg ttagagggtg 2002
cgggctttga gtgatgtgag accagcctga cctctgggga gggcatgggg ctggagactg 2062
atttcagtct caaggcgtcc tgtcaaggtc gctggacccc aaactcccct caaaggcaaa 2122
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aatttgatca tgcgcatagr ggtacctatc tggtggagac agaaggaggc actacattca 2362
gcagcatcct accagccggg gccagagcag gcaagatgga caatgctcca tcacctgaat 2422
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agaacaagac tccatctc                                              2920
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<210> 12
<211> 294
<212> PRT
<213> Homo sapiens

<400> 12

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Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp
 1               5                  10                  15
Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
            20                  25                  30
Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
        35                  40                  45
Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln
    50                  55                  60
Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn
65                  70                  75                  80
Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu
                85                  90                  95
Phe Asp Arg Lys Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His
            100                 105                 110
Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile
```

```
        115                 120                 125
Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu
    130                 135                 140
Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val
145                 150                 155                 160
Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro
                165                 170                 175
Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln
            180                 185                 190
Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu
        195                 200                 205
Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly
    210                 215                 220
Leu Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val
225                 230                 235                 240
Arg Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp
                245                 250                 255
Asp Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu
            260                 265                 270
Arg Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile
        275                 280                 285
Leu Gly Ile Thr Cys Ala
    290
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<210> 13
<211> 1095
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (113)...(661)

<221> misc_feature
<222> (0)...(0)
<223> ARP20

<400> 13

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ctggcaccct gtgcatcctt agccatagct tacaagagaa cagctggttg tg atg gca 118
                                                        Met Ala
                                                         1

gga ggc cct ccc aac acc aag gcg gag atg gaa atg tcc ctg gca gaa   166
Gly Gly Pro Pro Asn Thr Lys Ala Glu Met Glu Met Ser Leu Ala Glu
         5                  10                  15

gaa ctg aat cat gga cgc caa ggg gaa aac caa gag cac ctg gtg ata   214
Glu Leu Asn His Gly Arg Gln Gly Glu Asn Gln Glu His Leu Val Ile
     20                  25                  30

gca gaa atg atg gag ctt gga tct cgg tcc cgg ggt gcc tcc cag aag   262
Ala Glu Met Met Glu Leu Gly Ser Arg Ser Arg Gly Ala Ser Gln Lys
 35                  40                  45                  50
```

```
aag cag aag ttg gaa caa aaa gct gct ggc tct gct tca gcc aaa cga   310
Lys Gln Lys Leu Glu Gln Lys Ala Ala Gly Ser Ala Ser Ala Lys Arg
                 55                  60                  65

gtt tgg aat atg act gcc acc cga ccc aag aaa atg ggg tcc cag ctg   358
Val Trp Asn Met Thr Ala Thr Arg Pro Lys Lys Met Gly Ser Gln Leu
            70                  75                  80

cca aag ccc aga atg ctg aga gaa tca ggc cat ggg gat gcc cat ctc   406
Pro Lys Pro Arg Met Leu Arg Glu Ser Gly His Gly Asp Ala His Leu
        85                  90                  95

cag gag tac gct ggc aat ttc caa ggc ata cgt ttc cat tat gat cgc   454
Gln Glu Tyr Ala Gly Asn Phe Gln Gly Ile Arg Phe His Tyr Asp Arg
    100                 105                 110

aac cca ggg aca gat gca gtg gcg cag act agc ctg gaa gag ttc aat   502
Asn Pro Gly Thr Asp Ala Val Ala Gln Thr Ser Leu Glu Glu Phe Asn
115                 120                 125                 130

gta ctg gag atg gaa gtc atg aga aga cag ctg tat gca gtc aac cgg   550
Val Leu Glu Met Glu Val Met Arg Arg Gln Leu Tyr Ala Val Asn Arg
                135                 140                 145

cgt ctg cgc gcc ctg gag gaa cag ggc gcc acc tgg cgc cac agg gag   598
Arg Leu Arg Ala Leu Glu Glu Gln Gly Ala Thr Trp Arg His Arg Glu
            150                 155                 160

acc ctg atc atc gcc gtg ctg gtg tcg gcc agc att gcc aac ctg tgg   646
Thr Leu Ile Ile Ala Val Leu Val Ser Ala Ser Ile Ala Asn Leu Trp
        165                 170                 175

ctg tgg atg aac cag tgatcgcccc agcgcggcct ccgtattgga gccctccctg   701
Leu Trp Met Asn Gln
    180

cttccccttc tttctttcct ctttccccag gccgccactg cccttgcccc tttcatctcc 761
cagcagccct caggagcgtc aggatcattt tcaactctgg ttaggcctcc tacctgggga 821
ggccaggtca ctgcactggg aggtcctggc tgctgcgaag ctggaggagg actgcgtggg 881
ctgagatgcc acccttttgaa gggtgaacag catggcggca tctgggcccc acagtaacac 941
ctagtggcaa ccttgccttc ctgacctcag cggcccttct gttccatcct ctgtgggcag 1001
gggtgtggct ttgttttcct ccctcgtttg cttccacctc gtgcacagcg ctctgcacag 1061
acaacacgct caataaaagt tcagccatag cagc                           1095

<210> 14
<211> 183
<212> PRT
<213> Homo sapiens

<400> 14
Met Ala Gly Gly Pro Pro Asn Thr Lys Ala Glu Met Glu Met Ser Leu
 1               5                  10                  15
Ala Glu Glu Leu Asn His Gly Arg Gln Gly Glu Asn Gln Glu His Leu
            20                  25                  30
```

```
Val Ile Ala Glu Met Met Glu Leu Gly Ser Arg Ser Arg Gly Ala Ser
        35                  40                  45
Gln Lys Lys Gln Lys Leu Glu Gln Lys Ala Ala Gly Ser Ala Ser Ala
    50                  55                  60
Lys Arg Val Trp Asn Met Thr Ala Thr Arg Pro Lys Lys Met Gly Ser
65                  70                  75                  80
Gln Leu Pro Lys Pro Arg Met Leu Arg Glu Ser Gly His Gly Asp Ala
                85                  90                  95
His Leu Gln Glu Tyr Ala Gly Asn Phe Gln Gly Ile Arg Phe His Tyr
            100                 105                 110
Asp Arg Asn Pro Gly Thr Asp Ala Val Ala Gln Thr Ser Leu Glu Glu
        115                 120                 125
Phe Asn Val Leu Glu Met Glu Val Met Arg Arg Gln Leu Tyr Ala Val
    130                 135                 140
Asn Arg Arg Leu Arg Ala Leu Glu Glu Gln Gly Ala Thr Trp Arg His
145                 150                 155                 160
Arg Glu Thr Leu Ile Ile Ala Val Leu Val Ser Ala Ser Ile Ala Asn
                165                 170                 175
Leu Trp Leu Trp Met Asn Gln
            180
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<210> 15
<211> 3007
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (38)...(1378)

<221> misc_feature
<222> (0)...(0)
<223> ARP24

<400> 15

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gattccatta ctggttgaac tatggcacaa ggataaa atg agt aaa gat tta ctt  55
                                          Met Ser Lys Asp Leu Leu
                                           1               5

ctg gga att gcg aga atc cag ctt tct aac atc ttg tct tca gaa aaa  103
Leu Gly Ile Ala Arg Ile Gln Leu Ser Asn Ile Leu Ser Ser Glu Lys
            10                  15                  20

act cgt ttt tta ggt tct aat ggt gaa cag tgt tgg cgt caa act tac  151
Thr Arg Phe Leu Gly Ser Asn Gly Glu Gln Cys Trp Arg Gln Thr Tyr
        25                  30                  35

agt gaa agt gtg cct gtt ata gca gca caa gga tca aat aac agg ata  199
Ser Glu Ser Val Pro Val Ile Ala Ala Gln Gly Ser Asn Asn Arg Ile
    40                  45                  50

gca gat ctt tct tac aca gtg act cta gaa gat tat gga cta gta aaa  247
Ala Asp Leu Ser Tyr Thr Val Thr Leu Glu Asp Tyr Gly Leu Val Lys
55                  60                  65                  70
```

```
atg cgt gag att ttt atc tct gat tca tct cag ggt gta tct gcc gta   295
Met Arg Glu Ile Phe Ile Ser Asp Ser Ser Gln Gly Val Ser Ala Val
                 75                  80                  85

cag caa aag ccg tct tct ctt cct cca gca cct tgt cct tca gag atc   343
Gln Gln Lys Pro Ser Ser Leu Pro Pro Ala Pro Cys Pro Ser Glu Ile
            90                  95                 100

cag aca gag cct cgt gaa acg tta gaa tac aaa gca gca ctt gag cta   391
Gln Thr Glu Pro Arg Glu Thr Leu Glu Tyr Lys Ala Ala Leu Glu Leu
        105                 110                 115

gaa atg tgg aag gag atg caa gaa gat ata ttt gaa aat cag ctg aag   439
Glu Met Trp Lys Glu Met Gln Glu Asp Ile Phe Glu Asn Gln Leu Lys
    120                 125                 130

cag aaa gaa ctg gct cat atg cag gct ctt gca gag gaa tgg aag aaa   487
Gln Lys Glu Leu Ala His Met Gln Ala Leu Ala Glu Glu Trp Lys Lys
135                 140                 145                 150

agg gac cga gaa aga gaa tca cta gta aag aaa aag gtg gct gaa tat   535
Arg Asp Arg Glu Arg Glu Ser Leu Val Lys Lys Lys Val Ala Glu Tyr
                155                 160                 165

act att cta gaa gga aaa ctt caa aaa act cta att gac ttg gag aag   583
Thr Ile Leu Glu Gly Lys Leu Gln Lys Thr Leu Ile Asp Leu Glu Lys
            170                 175                 180

cga gag cag cag ctt gct agt gtg gaa tca gag ctt caa aga gaa aaa   631
Arg Glu Gln Gln Leu Ala Ser Val Glu Ser Glu Leu Gln Arg Glu Lys
        185                 190                 195

aag gaa ctg caa tca gaa cgt cag cgg aac ctg caa gaa ctg cag gac   679
Lys Glu Leu Gln Ser Glu Arg Gln Arg Asn Leu Gln Glu Leu Gln Asp
    200                 205                 210

tct atc cgt agg gcc aaa gag gac tgt att cac caa gta gaa cta gaa   727
Ser Ile Arg Arg Ala Lys Glu Asp Cys Ile His Gln Val Glu Leu Glu
215                 220                 225                 230

agg tta aaa atc aaa cag ctc gaa gag gat aaa cac cgm ctt cag caa   775
Arg Leu Lys Ile Lys Gln Leu Glu Glu Asp Lys His Xaa Leu Gln Gln
                235                 240                 245

cag ctt aat gat gct gaa aat aag tat aag att tkg raa aaa gag ttc   823
Gln Leu Asn Asp Ala Glu Asn Lys Tyr Lys Ile Xaa Xaa Lys Glu Phe
            250                 255                 260

caa cag ttc aag gac cag caa aac aac awa cca gaa atc cgt cta cag   871
Gln Gln Phe Lys Asp Gln Gln Asn Asn Xaa Pro Glu Ile Arg Leu Gln
        265                 270                 275

tct gaa ata aat ctt ctc acc ttg gaa aag gtt gaa ctt gaa aga aag   919
Ser Glu Ile Asn Leu Leu Thr Leu Glu Lys Val Glu Leu Glu Arg Lys
```

```
    280                 285                 290

ttg gaa tct gca act aag tct aaa ctg cat tac aag cag cag tgg gga   967
Leu Glu Ser Ala Thr Lys Ser Lys Leu His Tyr Lys Gln Gln Trp Gly
295                 300                 305                 310

cga gct ttg aaa gaa ctt gcc aga ctt aaa cag agg gag caa gaa agt   1015
Arg Ala Leu Lys Glu Leu Ala Arg Leu Lys Gln Arg Glu Gln Glu Ser
                315                 320                 325

caa atg gct cgt ctt aaa aaa cag cag gaa gaa ttg gaa cag atg aga   1063
Gln Met Ala Arg Leu Lys Lys Gln Gln Glu Glu Leu Glu Gln Met Arg
            330                 335                 340

cta cgt tac ctt gcc gct gag gaa aaa gat aca gta aaa acc gag cga   1111
Leu Arg Tyr Leu Ala Ala Glu Glu Lys Asp Thr Val Lys Thr Glu Arg
        345                 350                 355

caa gaa ttg ttg gat ata aga aat gaa ttg aac agg tta agg caa caa   1159
Gln Glu Leu Leu Asp Ile Arg Asn Glu Leu Asn Arg Leu Arg Gln Gln
    360                 365                 370

gag caa aaa caa tac cag gat tcc aca gag att gca agt gga aaa aag   1207
Glu Gln Lys Gln Tyr Gln Asp Ser Thr Glu Ile Ala Ser Gly Lys Lys
375                 380                 385                 390

gat ggc ccc cat ggc agt gta ttg gaa gaa ggt ttg gat gat tat ttg   1255
Asp Gly Pro His Gly Ser Val Leu Glu Glu Gly Leu Asp Asp Tyr Leu
                395                 400                 405

act cgc ctg ata gaa gaa agg gat act ttg atg aga acg ggt gtg tat   1303
Thr Arg Leu Ile Glu Glu Arg Asp Thr Leu Met Arg Thr Gly Val Tyr
            410                 415                 420

aat cac gag gat cga ata ata agt gaa ctc gac cga cag atc aga gag   1351
Asn His Glu Asp Arg Ile Ile Ser Glu Leu Asp Arg Gln Ile Arg Glu
        425                 430                 435

att ttg gca aaa agc aat gcc agt aat taataacatt tggaaaagct         1398
Ile Leu Ala Lys Ser Asn Ala Ser Asn
    440                 445

ttatagagac tctaagtcta aattttaatt tctttgtaaa aacctcaaaa gtgaggaaaa 1458
tggatgtttt aaaatggtat tttcaatttt ttataagcaa aattttgtat gttattgtat 1518
agtatttatt tgatcttatt tactttatgc tacctctccc acactggttt tatttgtaat 1578
ttgcatttat atactcattt taaatgactt ttcagtgttt ttcatagttt ataatctgat 1638
ggctaactaa ctttcaaaac agcttttaac taagtttgtt gtaggagaaa tgactgcggt 1698
aatttccagt tctataatgt ttcatgttga gccaaaagag tatatcttgc actttaaaaa 1758
cactgcgtcc tattccattt gaatgtaaat tcttaaaagt tgagaccaat tgtaaccagt 1818
ttaactcatt ttagatgacc tttttttctt ataatatttg caagtgacaa gtttgaaaac 1878
aaagcaagat cagtgcagag aagccacatg acatgttggg tgacagattg gtcatttatt 1938
taaataaagt taatacagat taaatttgtt tcaagagcta ttgaattttc aaattttcag 1998
tgtatttata acttttaaga acatgaagta ttagcttaat atagttttct ctgttggttt 2058
cttcctcaag tttgcattgt tttcttttgt taaaattaga gatttctttt tattttccag 2118
ttatagtaat actagctgtc agcttaaacc ctctgtaata gaacatggaa acagacacat 2178
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aaagacatta gctgaaaaaa tagagtgaaa atcaactatt ttttactccc gctaatttca 2238
atcaatcgtt ttcaaaagcg cacgagattc actcattgga tttatgcagt gccctgtctg 2298
tataaaaact cttaagagtt cctttatatc atattcttca gagccaacat ttgtcctcaa 2358
agcaacgttt cccacctcct tttactgagt actgaaaaag ttttagcaaa gtcacagatt 2418
aggttgaatt tcaaaatata tgtactttaa aaagttctga tttccaaata taataaagtt 2478
aaaattaagt atatacttta ggaagttacc aataacttcc atcaaagcag agtaggatat 2538
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gtccctatat ttattatata ttttttcctt attaacagag tattaatcta gtaaaaaata 2658
acccagcagt aaataataaa gaaattactg aatgagagga taatgaatct gaatcatagc 2718
aggaatttgc aatattaatt atggttagct atttttctct cattgatttt tgtgccactt 2778
gaatggaaca gaagcaagcc ttatgttttg gaaggtctgc ggtaaaatgc tgtgactgtt 2838
tactttcaat tgcattgtgt gttgcctgtg actgctttca aacgctagag ggggcctctg 2898
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aagctctttt ggctattgta acttaacaaa taaaatcata attgtgtgc 3007

<210> 16
<211> 447
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 243, 258, 259, 272
<223> Xaa = Any Amino Acid

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Ile Leu Ser Ser Glu Lys Thr Arg Phe Leu Gly Ser Asn Gly Glu Gln
20 25 30
Cys Trp Arg Gln Thr Tyr Ser Glu Ser Val Pro Val Ile Ala Ala Gln
35 40 45
Gly Ser Asn Asn Arg Ile Ala Asp Leu Ser Tyr Thr Val Thr Leu Glu
50 55 60
Asp Tyr Gly Leu Val Lys Met Arg Glu Ile Phe Ile Ser Asp Ser Ser
65 70 75 80
Gln Gly Val Ser Ala Val Gln Gln Lys Pro Ser Ser Leu Pro Pro Ala
85 90 95
Pro Cys Pro Ser Glu Ile Gln Thr Glu Pro Arg Glu Thr Leu Glu Tyr
100 105 110
Lys Ala Ala Leu Glu Leu Glu Met Trp Lys Glu Met Gln Glu Asp Ile
115 120 125
Phe Glu Asn Gln Leu Lys Gln Lys Glu Leu Ala His Met Gln Ala Leu
130 135 140
Ala Glu Glu Trp Lys Lys Arg Asp Arg Glu Arg Glu Ser Leu Val Lys
145 150 155 160
Lys Lys Val Ala Glu Tyr Thr Ile Leu Glu Gly Lys Leu Gln Lys Thr
165 170 175
Leu Ile Asp Leu Glu Lys Arg Glu Gln Gln Leu Ala Ser Val Glu Ser
180 185 190
Glu Leu Gln Arg Glu Lys Lys Glu Leu Gln Ser Glu Arg Gln Arg Asn
195 200 205
Leu Gln Glu Leu Gln Asp Ser Ile Arg Arg Ala Lys Glu Asp Cys Ile
210 215 220
His Gln Val Glu Leu Glu Arg Leu Lys Ile Lys Gln Leu Glu Glu Asp

```
225                 230                 235                 240
Lys His Xaa Leu Gln Gln Gln Leu Asn Asp Ala Glu Asn Lys Tyr Lys
                245                 250                 255
Ile Xaa Xaa Lys Glu Phe Gln Gln Phe Lys Asp Gln Gln Asn Asn Xaa
            260                 265                 270
Pro Glu Ile Arg Leu Gln Ser Glu Ile Asn Leu Leu Thr Leu Glu Lys
        275                 280                 285
Val Glu Leu Glu Arg Lys Leu Glu Ser Ala Thr Lys Ser Lys Leu His
    290                 295                 300
Tyr Lys Gln Gln Trp Gly Arg Ala Leu Lys Glu Leu Ala Arg Leu Lys
305                 310                 315                 320
Gln Arg Glu Gln Glu Ser Gln Met Ala Arg Leu Lys Lys Gln Gln Glu
                325                 330                 335
Glu Leu Glu Gln Met Arg Leu Arg Tyr Leu Ala Ala Glu Glu Lys Asp
            340                 345                 350
Thr Val Lys Thr Glu Arg Gln Glu Leu Leu Asp Ile Arg Asn Glu Leu
        355                 360                 365
Asn Arg Leu Arg Gln Gln Glu Gln Lys Gln Tyr Gln Asp Ser Thr Glu
    370                 375                 380
Ile Ala Ser Gly Lys Lys Asp Gly Pro His Gly Ser Val Leu Glu Glu
385                 390                 395                 400
Gly Leu Asp Asp Tyr Leu Thr Arg Leu Ile Glu Glu Arg Asp Thr Leu
                405                 410                 415
Met Arg Thr Gly Val Tyr Asn His Glu Asp Arg Ile Ile Ser Glu Leu
            420                 425                 430
Asp Arg Gln Ile Arg Glu Ile Leu Ala Lys Ser Asn Ala Ser Asn
        435                 440                 445
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<210> 17
<211> 3937
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (240)...(1013)

<221> misc_feature
<222> (0)...(0)
<223> ARP26

<400> 17

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cgaccgctgt cctccaacag cgcagggcag agcggctggc gccgccggag cgcggagcca 60
cgaccctccc tggccgcctt tgtctactgg ccgtgcggcc cggaaccgcc actctccagg 120
gccggggacg cgcccgcagc tgtcggtgac agctcctccc taccgcaacc ctccggggcg 180
gaggggcggt cgggccgggc cctgctagcc cgcgaccgca agcccgcgct cgcggatcg  239
atg ccc ccg cag cag ggg gac ccc gcg ttc ccc gac cgc tgc gag gcg   287
Met Pro Pro Gln Gln Gly Asp Pro Ala Phe Pro Asp Arg Cys Glu Ala
 1               5                  10                  15

cct ccg gtg ccg ccg cgt cgg gag cgc ggt gga cgc ggg gga cgc ggg   335
Pro Pro Val Pro Pro Arg Arg Glu Arg Gly Gly Arg Gly Gly Arg Gly
            20                  25                  30
```

```
cct ggg gag ccg ggg ggc cgg ggg cgt gcg ggg ggt gcc gag ggg cgc   383
Pro Gly Glu Pro Gly Gly Arg Gly Arg Ala Gly Gly Ala Glu Gly Arg
          35                  40                  45

ggc gtc aag tgc gtg ctg gtc ggc gac ggc gcg gtg ggc aag acg agc   431
Gly Val Lys Cys Val Leu Val Gly Asp Gly Ala Val Gly Lys Thr Ser
     50                  55                  60

ctg gtg gtg agc tac acc acc aac ggc tac ccc acc gag tac atc cct   479
Leu Val Val Ser Tyr Thr Thr Asn Gly Tyr Pro Thr Glu Tyr Ile Pro
 65                  70                  75                  80

act gcc ttc gac aac ttc tcc gcg gtg gtg tct gtg gat ggg cgg ccc   527
Thr Ala Phe Asp Asn Phe Ser Ala Val Val Ser Val Asp Gly Arg Pro
                 85                  90                  95

gtg aga ctc caa ctc tgt gac act gcc gga cag gat gaa ttt gac aag   575
Val Arg Leu Gln Leu Cys Asp Thr Ala Gly Gln Asp Glu Phe Asp Lys
            100                 105                 110

ctg agg cct ctc tgc tac acc aac aca gac atc ttc ctg ctc tgc ttc   623
Leu Arg Pro Leu Cys Tyr Thr Asn Thr Asp Ile Phe Leu Leu Cys Phe
        115                 120                 125

agt gtc gtg agc ccc tca tcc ttc cag aac gtc agt gag aaa tgg gtg   671
Ser Val Val Ser Pro Ser Ser Phe Gln Asn Val Ser Glu Lys Trp Val
    130                 135                 140

ccg gag att cga tgc cac tgt ccc aaa gcc ccc atc atc cta gtt gga   719
Pro Glu Ile Arg Cys His Cys Pro Lys Ala Pro Ile Ile Leu Val Gly
145                 150                 155                 160

acg cag tcg gat ctc aga gaa gat gtc aaa gtc ctc att gag ttg gac   767
Thr Gln Ser Asp Leu Arg Glu Asp Val Lys Val Leu Ile Glu Leu Asp
                165                 170                 175

aaa tgc aaa gaa aag cca gtg cct gaa gag gcg gct aag ctg tgc gcc   815
Lys Cys Lys Glu Lys Pro Val Pro Glu Glu Ala Ala Lys Leu Cys Ala
            180                 185                 190

gag gaa atc aaa gcc gcc tcc tac atc gag tgt tca gcc ttg act caa   863
Glu Glu Ile Lys Ala Ala Ser Tyr Ile Glu Cys Ser Ala Leu Thr Gln
        195                 200                 205

aaa aac ctc aaa gag gtc ttt gat gca gcc atc gtc gct ggc att caa   911
Lys Asn Leu Lys Glu Val Phe Asp Ala Ala Ile Val Ala Gly Ile Gln
    210                 215                 220

tac tcg gac act cag caa cag cca aag aag tct aaa agc agg act cca   959
Tyr Ser Asp Thr Gln Gln Gln Pro Lys Lys Ser Lys Ser Arg Thr Pro
225                 230                 235                 240

gat aaa atg aaa aac ctc tcc aag tcc tgg tgg aag aag tac tgc tgt   1007
Asp Lys Met Lys Asn Leu Ser Lys Ser Trp Trp Lys Lys Tyr Cys Cys
                245                 250                 255
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ttc gta tgatgctggc aagacaccca gaaaggctat tttcagatga aatcgatatt 1063
Phe Val

agaagctata ttagctgaaa caactccttt tactgcgtag aacctatatc gagagtgtgt 1123
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Gly Val Lys Cys Val Leu Val Gly Asp Gly Ala Val Gly Lys Thr Ser
50 55 60
Leu Val Val Ser Tyr Thr Thr Asn Gly Tyr Pro Thr Glu Tyr Ile Pro
65 70 75 80
Thr Ala Phe Asp Asn Phe Ser Ala Val Val Ser Val Asp Gly Arg Pro
85 90 95
Val Arg Leu Gln Leu Cys Asp Thr Ala Gly Gln Asp Glu Phe Asp Lys
100 105 110
Leu Arg Pro Leu Cys Tyr Thr Asn Thr Asp Ile Phe Leu Leu Cys Phe
115 120 125
Ser Val Val Ser Pro Ser Ser Phe Gln Asn Val Ser Glu Lys Trp Val
130 135 140
Pro Glu Ile Arg Cys His Cys Pro Lys Ala Pro Ile Ile Leu Val Gly
145 150 155 160
Thr Gln Ser Asp Leu Arg Glu Asp Val Lys Val Leu Ile Glu Leu Asp
165 170 175
Lys Cys Lys Glu Lys Pro Val Pro Glu Glu Ala Ala Lys Leu Cys Ala
180 185 190
Glu Glu Ile Lys Ala Ala Ser Tyr Ile Glu Cys Ser Ala Leu Thr Gln
195 200 205
Lys Asn Leu Lys Glu Val Phe Asp Ala Ala Ile Val Ala Gly Ile Gln
210 215 220
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225 230 235 240
Asp Lys Met Lys Asn Leu Ser Lys Ser Trp Trp Lys Lys Tyr Cys Cys
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Ser Gly Ser Val Gly Ser Gln Ala Val Ala Arg Arg Met Asp Gly Asp
 5                  10                  15                  20

agc cga gat ggc ggc ggc ggc aag gac gcc acc ggg tcg gag gac tac  152
Ser Arg Asp Gly Gly Gly Gly Lys Asp Ala Thr Gly Ser Glu Asp Tyr
                25                  30                  35

gag aac ctg ccg act agc gcc tcc gtg tcc acc cac atg aca gca gga  200
Glu Asn Leu Pro Thr Ser Ala Ser Val Ser Thr His Met Thr Ala Gly
            40                  45                  50

gcg atg gcc ggg atc ctg gag cac tcg gtc atg tac ccg gtg gac tcg  248
Ala Met Ala Gly Ile Leu Glu His Ser Val Met Tyr Pro Val Asp Ser
        55                  60                  65

gtg aag aca cga atg cag agt ttg agt cca gat ccc aaa gcc cag tac  296
Val Lys Thr Arg Met Gln Ser Leu Ser Pro Asp Pro Lys Ala Gln Tyr
    70                  75                  80

aca agt atc tac gga gcc ctc aag aaa atc atg cgg acc gaa ggc ttc  344
Thr Ser Ile Tyr Gly Ala Leu Lys Lys Ile Met Arg Thr Glu Gly Phe
 85                  90                  95                 100

tgg agg ccc ttg cga ggc gtc aac gtc atg atc atg ggt gca ggg ccg  392
Trp Arg Pro Leu Arg Gly Val Asn Val Met Ile Met Gly Ala Gly Pro
                105                 110                 115

gcc cat gcc atg tat ttt gcc tgc tat gaa aac atg aaa agg act tta  440
Ala His Ala Met Tyr Phe Ala Cys Tyr Glu Asn Met Lys Arg Thr Leu
            120                 125                 130

aat gac gtt ttc cac cac caa gga aac agc cac cta gcc aac ggg ata  488
Asn Asp Val Phe His His Gln Gly Asn Ser His Leu Ala Asn Gly Ile
        135                 140                 145

gct ggg agt atg gcc acc ctg ctc cac gat gcg gta atg aat cca gca  536
Ala Gly Ser Met Ala Thr Leu Leu His Asp Ala Val Met Asn Pro Ala
    150                 155                 160

gaa gtg gtg aag cag cgc ttg cag atg tac aac tcg cag cac cgg tca  584
Glu Val Val Lys Gln Arg Leu Gln Met Tyr Asn Ser Gln His Arg Ser
165                 170                 175                 180

gca atc agc tgc atc cgg acg gtg tgg agg acc gag ggg ttg ggg gcc  632
Ala Ile Ser Cys Ile Arg Thr Val Trp Arg Thr Glu Gly Leu Gly Ala
                185                 190                 195

ttc tac cgg agc tac acc acg cag ctg acc atg aac atc ccc ttc cag  680
Phe Tyr Arg Ser Tyr Thr Thr Gln Leu Thr Met Asn Ile Pro Phe Gln
            200                 205                 210
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tcc atc cac ttc atc acc tat gag ttc ctg cag gag cag gtc aac ccc   728
Ser Ile His Phe Ile Thr Tyr Glu Phe Leu Gln Glu Gln Val Asn Pro
        215                 220                 225

cac cgg acc tac aac ccg cag tcc cac atc atc tca ggc ggg ctg gcc   776
His Arg Thr Tyr Asn Pro Gln Ser His Ile Ile Ser Gly Gly Leu Ala
    230                 235                 240

ggg gcc ctc gcc gcg gcc gcc acg acc ccc ctg gac gtc tgt aag acc   824
Gly Ala Leu Ala Ala Ala Ala Thr Thr Pro Leu Asp Val Cys Lys Thr
245                 250                 255                 260

ctt ctg aac act cag gag aac gtg gcc ctc tcg ctg gcc aac atc agc   872
Leu Leu Asn Thr Gln Glu Asn Val Ala Leu Ser Leu Ala Asn Ile Ser
                265                 270                 275

ggc cgg ctg tcg ggt atg gcc aat gcc ttc cgg acg gtg tac cag ctc   920
Gly Arg Leu Ser Gly Met Ala Asn Ala Phe Arg Thr Val Tyr Gln Leu
            280                 285                 290

aac ggc ctg ccg gct act tca aag gca tcc agg cgc gtg tca tct acc   968
Asn Gly Leu Pro Ala Thr Ser Lys Ala Ser Arg Arg Val Ser Ser Thr
        295                 300                 305

aga tgc cct cca ccg cca ttt ctt ggt ctg tct atg agt tct tca agt   1016
Arg Cys Pro Pro Pro Pro Phe Leu Gly Leu Ser Met Ser Ser Ser Ser
    310                 315                 320

act ttc tca cca agc gcc agc tgg aaa atc gag ctc cat act aaa gga   1064
Thr Phe Ser Pro Ser Ala Ser Trp Lys Ile Glu Leu His Thr Lys Gly
325                 330                 335                 340

agg gat cat aga atc ttt tct taaagtcatt ctctgcctgc atccagcccc      1115
Arg Asp His Arg Ile Phe Ser
                345

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            20                  25                  30
Ser Glu Asp Tyr Glu Asn Leu Pro Thr Ser Ala Ser Val Ser Thr His
        35                  40                  45
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Met Thr Ala Gly Ala Met Ala Gly Ile Leu Glu His Ser Val Met Tyr
    50                  55                  60
Pro Val Asp Ser Val Lys Thr Arg Met Gln Ser Leu Ser Pro Asp Pro
65                  70                  75                  80
Lys Ala Gln Tyr Thr Ser Ile Tyr Gly Ala Leu Lys Lys Ile Met Arg
                85                  90                  95
Thr Glu Gly Phe Trp Arg Pro Leu Arg Gly Val Asn Val Met Ile Met
            100                 105                 110
Gly Ala Gly Pro Ala His Ala Met Tyr Phe Ala Cys Tyr Glu Asn Met
        115                 120                 125
Lys Arg Thr Leu Asn Asp Val Phe His His Gln Gly Asn Ser His Leu
    130                 135                 140
Ala Asn Gly Ile Ala Gly Ser Met Ala Thr Leu Leu His Asp Ala Val
145                 150                 155                 160
Met Asn Pro Ala Glu Val Val Lys Gln Arg Leu Gln Met Tyr Asn Ser
                165                 170                 175
Gln His Arg Ser Ala Ile Ser Cys Ile Arg Thr Val Trp Arg Thr Glu
            180                 185                 190
Gly Leu Gly Ala Phe Tyr Arg Ser Tyr Thr Thr Gln Leu Thr Met Asn
        195                 200                 205
Ile Pro Phe Gln Ser Ile His Phe Ile Thr Tyr Glu Phe Leu Gln Glu
    210                 215                 220
Gln Val Asn Pro His Arg Thr Tyr Asn Pro Gln Ser His Ile Ile Ser
225                 230                 235                 240
Gly Gly Leu Ala Gly Ala Leu Ala Ala Ala Ala Thr Thr Pro Leu Asp
                245                 250                 255
Val Cys Lys Thr Leu Leu Asn Thr Gln Glu Asn Val Ala Leu Ser Leu
            260                 265                 270
Ala Asn Ile Ser Gly Arg Leu Ser Gly Met Ala Asn Ala Phe Arg Thr
        275                 280                 285
Val Tyr Gln Leu Asn Gly Leu Pro Ala Thr Ser Lys Ala Ser Arg Arg
    290                 295                 300
Val Ser Ser Thr Arg Cys Pro Pro Pro Pro Phe Leu Gly Leu Ser Met
305                 310                 315                 320
Ser Ser Ser Ser Thr Phe Ser Pro Ser Ala Ser Trp Lys Ile Glu Leu
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His Thr Lys Gly Arg Asp His Arg Ile Phe Ser
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ggacattgtt cacttcccct cgcttcccct ctagaagccc cctttgccat ccctgcacct 240
tgtttcgggt g atg ccc gag agg gag ctg tgg cca gcg ggg act ggc tca  290
             Met Pro Glu Arg Glu Leu Trp Pro Ala Gly Thr Gly Ser
              1               5                  10

gaa ccc gtg acc cgt gtc ggc agc tgt gac agc atg atg agc agc acc   338
Glu Pro Val Thr Arg Val Gly Ser Cys Asp Ser Met Met Ser Ser Thr
     15                  20                  25

tcc acc cgc tct gga tct agt gat agc agc tac gac ttc ctg tcc act   386
Ser Thr Arg Ser Gly Ser Ser Asp Ser Ser Tyr Asp Phe Leu Ser Thr
 30                  35                  40                  45

gaa gag aag gag tgt ctg ctc ttc ctg gag gag acc att ggc tca ctg   434
Glu Glu Lys Glu Cys Leu Leu Phe Leu Glu Glu Thr Ile Gly Ser Leu
                 50                  55                  60

gac acg gag gct gac agc gga ctg tcc act gac gag tct gag cca gcc   482
Asp Thr Glu Ala Asp Ser Gly Leu Ser Thr Asp Glu Ser Glu Pro Ala
             65                  70                  75

aca act ccc aga ggt ttc cga gca ctg ccc ata acc caa ccc act ccc   530
Thr Thr Pro Arg Gly Phe Arg Ala Leu Pro Ile Thr Gln Pro Thr Pro
         80                  85                  90

cgg gga ggt cca gag gag acc atc act cag caa gga cga acg cca agg   578
Arg Gly Gly Pro Glu Glu Thr Ile Thr Gln Gln Gly Arg Thr Pro Arg
     95                  100                 105

aca gta act gag tcc agc tca tcc cac cct cct gag ccc cag ggc cta   626
Thr Val Thr Glu Ser Ser Ser Ser His Pro Pro Glu Pro Gln Gly Leu
110                 115                 120                 125

ggc ctc agg tct ggc tcc tac agc ctc cct agg aat atc cac att gcc   674
Gly Leu Arg Ser Gly Ser Tyr Ser Leu Pro Arg Asn Ile His Ile Ala
                130                 135                 140

aga agc cag aac ttc agg aaa agc acc acc cag gct agc agt cac aac   722
Arg Ser Gln Asn Phe Arg Lys Ser Thr Thr Gln Ala Ser Ser His Asn
            145                 150                 155

cct gga gaa ccg ggg agg ctt gcg cca gag cct gag aaa gaa cag gtc   770
Pro Gly Glu Pro Gly Arg Leu Ala Pro Glu Pro Glu Lys Glu Gln Val
        160                 165                 170

agc cag agc agc caa ccc agg cag gca cct gcc agc ccc cag gag gct   818
Ser Gln Ser Ser Gln Pro Arg Gln Ala Pro Ala Ser Pro Gln Glu Ala
    175                 180                 185

gcc ctt gac ttg gac gtg gtg ctc atc cct ccg cca gaa gct ttc cgg   866
Ala Leu Asp Leu Asp Val Val Leu Ile Pro Pro Pro Glu Ala Phe Arg
190                 195                 200                 205
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gac acc cag cca gag cag tgt agg gaa gcc agc ctg ccc gag ggg cca   914
Asp Thr Gln Pro Glu Gln Cys Arg Glu Ala Ser Leu Pro Glu Gly Pro
                210                 215                 220

gga cag cag ggc cac aca ccc cag ctc cac aca cca tcc agc tcc cag   962
Gly Gln Gln Gly His Thr Pro Gln Leu His Thr Pro Ser Ser Ser Gln
            225                 230                 235

gaa aga gag cag act cct tca gaa gcc atg tcc caa aaa gcc aag gaa   1010
Glu Arg Glu Gln Thr Pro Ser Glu Ala Met Ser Gln Lys Ala Lys Glu
        240                 245                 250

aca gtc tca acc agg tac aca caa ccc cag cct cct cct gca ggg ttg   1058
Thr Val Ser Thr Arg Tyr Thr Gln Pro Gln Pro Pro Pro Ala Gly Leu
    255                 260                 265

cct cag aat gca aga gct gaa gat gct ccc ctc tca tca ggg gag gac   1106
Pro Gln Asn Ala Arg Ala Glu Asp Ala Pro Leu Ser Ser Gly Glu Asp
270                 275                 280                 285

cca aac agc cga cta gct ccc ctc aca acc cct aag ccc cgg aag ctg   1154
Pro Asn Ser Arg Leu Ala Pro Leu Thr Thr Pro Lys Pro Arg Lys Leu
                290                 295                 300

cca cct aat att gtt ctg aag agc agc cga agc agt ttc cac agt gac   1202
Pro Pro Asn Ile Val Leu Lys Ser Ser Arg Ser Ser Phe His Ser Asp
            305                 310                 315

ccc cag cac tgg ctg tcc cgc cac act gag gct gcc cct gga gat tct   1250
Pro Gln His Trp Leu Ser Arg His Thr Glu Ala Ala Pro Gly Asp Ser
        320                 325                 330

ggc ctg atc tcc tgt tca ctg caa gag cag aga aaa gca cgt aaa gaa   1298
Gly Leu Ile Ser Cys Ser Leu Gln Glu Gln Arg Lys Ala Arg Lys Glu
    335                 340                 345

gct cta gag aag ctg ggg cta ccc cag gat caa gat gag cct gga ctc   1346
Ala Leu Glu Lys Leu Gly Leu Pro Gln Asp Gln Asp Glu Pro Gly Leu
350                 355                 360                 365

cac tta agt aag ccc acc agc tcc atc aga ccc aag gag aca cgg gcc   1394
His Leu Ser Lys Pro Thr Ser Ser Ile Arg Pro Lys Glu Thr Arg Ala
                370                 375                 380

cag cat ctg tcc cca gct cca ggt ctg gct cag cct gca gct cca gcc   1442
Gln His Leu Ser Pro Ala Pro Gly Leu Ala Gln Pro Ala Ala Pro Ala
            385                 390                 395

cag gcc tca gca gct att cct gct gct ggg aag gct ctg gct caa gct   1490
Gln Ala Ser Ala Ala Ile Pro Ala Ala Gly Lys Ala Leu Ala Gln Ala
        400                 405                 410

ccg gct cca gct cca ggt cca gct cag gga cct ttg cca atg aag tct   1538
Pro Ala Pro Ala Pro Gly Pro Ala Gln Gly Pro Leu Pro Met Lys Ser
    415                 420                 425
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cca gct cca ggc aat gtt gca gct agc aaa tct atg cca att cct atc   1586
Pro Ala Pro Gly Asn Val Ala Ala Ser Lys Ser Met Pro Ile Pro Ile
430                 435                 440                 445

cct aag gcc cca agg gca aac agt gcc ctg act cca ccg aag cca gag   1634
Pro Lys Ala Pro Arg Ala Asn Ser Ala Leu Thr Pro Pro Lys Pro Glu
                450                 455                 460

tca ggg ctg act ctc cag gag agc aac acc cct ggc ctg aga cag atg   1682
Ser Gly Leu Thr Leu Gln Glu Ser Asn Thr Pro Gly Leu Arg Gln Met
            465                 470                 475

aac ttc aag tcc aac act ctg gag cgc tca ggc gtg gga ctg agc agc   1730
Asn Phe Lys Ser Asn Thr Leu Glu Arg Ser Gly Val Gly Leu Ser Ser
        480                 485                 490

tac ctt tca act gag aaa gat gcc agc ccc aaa acc agc act tct ctg   1778
Tyr Leu Ser Thr Glu Lys Asp Ala Ser Pro Lys Thr Ser Thr Ser Leu
    495                 500                 505

gga aag ggc tcc ttc ttg gac aag atc tcg ccc agt gtc tta cgt aat   1826
Gly Lys Gly Ser Phe Leu Asp Lys Ile Ser Pro Ser Val Leu Arg Asn
510                 515                 520                 525

tct cgg ccc cgc ccg gcc tcc ctg ggc acg ggg aaa gat ttt gca ggt   1874
Ser Arg Pro Arg Pro Ala Ser Leu Gly Thr Gly Lys Asp Phe Ala Gly
                530                 535                 540

atc cag gta ggc aag ctg gct gac ctg gag cag gag cag agc tcc aag   1922
Ile Gln Val Gly Lys Leu Ala Asp Leu Glu Gln Glu Gln Ser Ser Lys
            545                 550                 555

cgc ctg tcc tac caa gga cag agc cgt gac aag ctt cct cgc ccc ccc   1970
Arg Leu Ser Tyr Gln Gly Gln Ser Arg Asp Lys Leu Pro Arg Pro Pro
        560                 565                 570

tgt gtc agt gtc aag atc tcc cca aag ggt gtc ccc aat gaa cac aga   2018
Cys Val Ser Val Lys Ile Ser Pro Lys Gly Val Pro Asn Glu His Arg
    575                 580                 585

agg gag gcc ctg aag aag ctg gga ctg ttg aag gag tagactctgc        2064
Arg Glu Ala Leu Lys Lys Leu Gly Leu Leu Lys Glu
590                 595                 600

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Ser Gly Ser Ser Asp Ser Ser Tyr Asp Phe Leu Ser Thr Glu Glu Lys
35 40 45
Glu Cys Leu Leu Phe Leu Glu Glu Thr Ile Gly Ser Leu Asp Thr Glu
50 55 60
Ala Asp Ser Gly Leu Ser Thr Asp Glu Ser Glu Pro Ala Thr Thr Pro
65 70 75 80
Arg Gly Phe Arg Ala Leu Pro Ile Thr Gln Pro Thr Pro Arg Gly Gly
85 90 95
Pro Glu Glu Thr Ile Thr Gln Gln Gly Arg Thr Pro Arg Thr Val Thr
100 105 110
Glu Ser Ser Ser Ser His Pro Pro Glu Pro Gln Gly Leu Gly Leu Arg
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Ser Gly Ser Tyr Ser Leu Pro Arg Asn Ile His Ile Ala Arg Ser Gln
130 135 140
Asn Phe Arg Lys Ser Thr Thr Gln Ala Ser Ser His Asn Pro Gly Glu
145 150 155 160
Pro Gly Arg Leu Ala Pro Glu Pro Glu Lys Glu Gln Val Ser Gln Ser
165 170 175
Ser Gln Pro Arg Gln Ala Pro Ala Ser Pro Gln Glu Ala Ala Leu Asp
180 185 190
Leu Asp Val Val Leu Ile Pro Pro Pro Glu Ala Phe Arg Asp Thr Gln
195 200 205
Pro Glu Gln Cys Arg Glu Ala Ser Leu Pro Glu Gly Pro Gly Gln Gln
210 215 220
Gly His Thr Pro Gln Leu His Thr Pro Ser Ser Ser Gln Glu Arg Glu
225 230 235 240
Gln Thr Pro Ser Glu Ala Met Ser Gln Lys Ala Lys Glu Thr Val Ser
245 250 255
Thr Arg Tyr Thr Gln Pro Gln Pro Pro Pro Ala Gly Leu Pro Gln Asn
260 265 270
Ala Arg Ala Glu Asp Ala Pro Leu Ser Ser Gly Glu Asp Pro Asn Ser
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Arg Leu Ala Pro Leu Thr Thr Pro Lys Pro Arg Lys Leu Pro Pro Asn

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Ile Val Leu Lys Ser Ser Arg Ser Ser Phe His Ser Asp Pro Gln His
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Ser Cys Ser Leu Gln Glu Gln Arg Lys Ala Arg Lys Glu Ala Leu Glu
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Lys Leu Gly Leu Pro Gln Asp Gln Asp Glu Pro Gly Leu His Leu Ser
        355                 360                 365
Lys Pro Thr Ser Ser Ile Arg Pro Lys Glu Thr Arg Ala Gln His Leu
    370                 375                 380
Ser Pro Ala Pro Gly Leu Ala Gln Pro Ala Ala Pro Ala Gln Ala Ser
385                 390                 395                 400
Ala Ala Ile Pro Ala Ala Gly Lys Ala Leu Ala Gln Ala Pro Ala Pro
                405                 410                 415
Ala Pro Gly Pro Ala Gln Gly Pro Leu Pro Met Lys Ser Pro Ala Pro
            420                 425                 430
Gly Asn Val Ala Ala Ser Lys Ser Met Pro Ile Pro Ile Pro Lys Ala
        435                 440                 445
Pro Arg Ala Asn Ser Ala Leu Thr Pro Pro Lys Pro Glu Ser Gly Leu
    450                 455                 460
Thr Leu Gln Glu Ser Asn Thr Pro Gly Leu Arg Gln Met Asn Phe Lys
465                 470                 475                 480
Ser Asn Thr Leu Glu Arg Ser Gly Val Gly Leu Ser Ser Tyr Leu Ser
                485                 490                 495
Thr Glu Lys Asp Ala Ser Pro Lys Thr Ser Thr Ser Leu Gly Lys Gly
            500                 505                 510
Ser Phe Leu Asp Lys Ile Ser Pro Ser Val Leu Arg Asn Ser Arg Pro
        515                 520                 525
Arg Pro Ala Ser Leu Gly Thr Gly Lys Asp Phe Ala Gly Ile Gln Val
    530                 535                 540
Gly Lys Leu Ala Asp Leu Glu Gln Glu Gln Ser Ser Lys Arg Leu Ser
545                 550                 555                 560
Tyr Gln Gly Gln Ser Arg Asp Lys Leu Pro Arg Pro Pro Cys Val Ser
                565                 570                 575
Val Lys Ile Ser Pro Lys Gly Val Pro Asn Glu His Arg Arg Glu Ala
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Leu Lys Lys Leu Gly Leu Leu Lys Glu
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tgaacattta tagcatttat ttcccaaatc tgttaac atg gca aaa tat gtc agt  115
                                          Met Ala Lys Tyr Val Ser
                                           1               5

ctc act gaa gct aac gaa gaa ctc aag gtc tta atg gac gag aac cag   163
Leu Thr Glu Ala Asn Glu Glu Leu Lys Val Leu Met Asp Glu Asn Gln
            10                  15                  20

acc agc cgc ccc gtg gcc gtt cac acc tcc acc gtg aac ccg ctc ggg   211
Thr Ser Arg Pro Val Ala Val His Thr Ser Thr Val Asn Pro Leu Gly
        25                  30                  35

aag cag ctc ttg ccg aaa acc ttt gga cag tcc agt gtc aac att gac   259
Lys Gln Leu Leu Pro Lys Thr Phe Gly Gln Ser Ser Val Asn Ile Asp
    40                  45                  50

cag caa gtg gta att ggg tat gcc tca gag acc agc agc atc aaa cat   307
Gln Gln Val Val Ile Gly Tyr Ala Ser Glu Thr Ser Ser Ile Lys His
55                  60                  65                  70

ccc tgt ggt agg aag ccc aaa ccc acc cag cac tca ctt tgc ctc tca   355
Pro Cys Gly Arg Lys Pro Lys Pro Thr Gln His Ser Leu Cys Leu Ser
                75                  80                  85

gaa cca gca ttc cta ctc ctc acc tcc ttg ggc cgg cag cac aac agg   403
Glu Pro Ala Phe Leu Leu Leu Thr Ser Leu Gly Arg Gln His Asn Arg
            90                  95                  100

aaa gga gag aag aat ggc atg ggc ctg tgc cgt ctt tcc atg aag gtc   451
Lys Gly Glu Lys Asn Gly Met Gly Leu Cys Arg Leu Ser Met Lys Val
        105                 110                 115

tgg gag acg gtg cag agg aaa ggg acc act tcc tgc cag gaa gtg gtg   499
Trp Glu Thr Val Gln Arg Lys Gly Thr Thr Ser Cys Gln Glu Val Val
    120                 125                 130

ggc gag ctg gtc gcc aag ttc aga gct gcc agc aac cac gcc tca cca   547
Gly Glu Leu Val Ala Lys Phe Arg Ala Ala Ser Asn His Ala Ser Pro
135                 140                 145                 150

aac gag tca gct tat gac gtg aaa aac ata aaa cgg cgc acc tac gat   595
Asn Glu Ser Ala Tyr Asp Val Lys Asn Ile Lys Arg Arg Thr Tyr Asp
                155                 160                 165

gcc tta aac gtg ctg atg gcc atg aat atc atc tcc agg gag aaa aag   643
Ala Leu Asn Val Leu Met Ala Met Asn Ile Ile Ser Arg Glu Lys Lys
            170                 175                 180

aag atc aag tgg att ggt ctg acc acc aac tcg gct cag aac tgt cag   691
Lys Ile Lys Trp Ile Gly Leu Thr Thr Asn Ser Ala Gln Asn Cys Gln
        185                 190                 195

aac tta cgg gtg gaa aga cag aag aga ctt gaa aga ata aag cag aaa   739
Asn Leu Arg Val Glu Arg Gln Lys Arg Leu Glu Arg Ile Lys Gln Lys
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cag tct gaa ctt caa caa ctt att cta cag caa att gct ttc aag aac   787
Gln Ser Glu Leu Gln Gln Leu Ile Leu Gln Gln Ile Ala Phe Lys Asn
215                 220                 225                 230

ctg gtg ctg aga aac cag tat gtg gag gag cag gtc agc cag cgg ccg   835
Leu Val Leu Arg Asn Gln Tyr Val Glu Glu Gln Val Ser Gln Arg Pro
                235                 240                 245

ctg ccc aac tca gtc atc cac gtg ccc ttc atc atc atc agc agt agc   883
Leu Pro Asn Ser Val Ile His Val Pro Phe Ile Ile Ile Ser Ser Ser
            250                 255                 260

aag aag acc gtc atc aac tgc agc atc tcc gac gac aaa tca gaa tat   931
Lys Lys Thr Val Ile Asn Cys Ser Ile Ser Asp Asp Lys Ser Glu Tyr
        265                 270                 275

ctg ttt aag ttt aac agc tcc ttt gaa atc cac gat gac aca gaa gtg   979
Leu Phe Lys Phe Asn Ser Ser Phe Glu Ile His Asp Asp Thr Glu Val
    280                 285                 290

ctg atg tgg atg ggc atg act ttt ggg cta gag tcc ggg agc tgc tct   1027
Leu Met Trp Met Gly Met Thr Phe Gly Leu Glu Ser Gly Ser Cys Ser
295                 300                 305                 310

gcc gaa gac ctt aaa atg gcc aga aat ttg gtc cca aag gct ctg gag   1075
Ala Glu Asp Leu Lys Met Ala Arg Asn Leu Val Pro Lys Ala Leu Glu
                315                 320                 325

ccg tac gtg aca gaa atg gct cag gga act ttt gga ggt gtg ttc acg   1123
Pro Tyr Val Thr Glu Met Ala Gln Gly Thr Phe Gly Gly Val Phe Thr
            330                 335                 340

acg gca ggt tcc agg tct aat ggc acg tgg ctt tct gcc agt gac ctg   1171
Thr Ala Gly Ser Arg Ser Asn Gly Thr Trp Leu Ser Ala Ser Asp Leu
        345                 350                 355

acc aac att gcg att ggg atg ctg gcc aca agc tcc ggt gga tct cag   1219
Thr Asn Ile Ala Ile Gly Met Leu Ala Thr Ser Ser Gly Gly Ser Gln
    360                 365                 370

tac agt ggc tcc agg gtg gag acc cca gca gtc gag gag gaa gag gag   1267
Tyr Ser Gly Ser Arg Val Glu Thr Pro Ala Val Glu Glu Glu Glu Glu
375                 380                 385                 390

gag gac aac aac gat gac gac ctc agt gag aat gac gag gat gac t     1313
Glu Asp Asn Asn Asp Asp Asp Leu Ser Glu Asn Asp Glu Asp Asp
                395                 400                 405

gacgtcctct cgccttaaga ttcagcttca ggaaaacatt tagggaaaag aaacttttt 1373
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ttaggatttt gtgttttcat tttctatttt tctttaaatg cagagttcat tgttgcccct 1613
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<212> PRT
<213> Homo sapiens

<400> 24

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Thr Val Asn Pro Leu Gly Lys Gln Leu Leu Pro Lys Thr Phe Gly Gln
        35                  40                  45
Ser Ser Val Asn Ile Asp Gln Gln Val Val Ile Gly Tyr Ala Ser Glu
    50                  55                  60
Thr Ser Ser Ile Lys His Pro Cys Gly Arg Lys Pro Lys Pro Thr Gln
65                  70                  75                  80
His Ser Leu Cys Leu Ser Glu Pro Ala Phe Leu Leu Leu Thr Ser Leu
                85                  90                  95
Gly Arg Gln His Asn Arg Lys Gly Glu Lys Asn Gly Met Gly Leu Cys
            100                 105                 110
Arg Leu Ser Met Lys Val Trp Glu Thr Val Gln Arg Lys Gly Thr Thr
        115                 120                 125
Ser Cys Gln Glu Val Val Gly Glu Leu Val Ala Lys Phe Arg Ala Ala
    130                 135                 140
Ser Asn His Ala Ser Pro Asn Glu Ser Ala Tyr Asp Val Lys Asn Ile
145                 150                 155                 160
Lys Arg Arg Thr Tyr Asp Ala Leu Asn Val Leu Met Ala Met Asn Ile
                165                 170                 175
Ile Ser Arg Glu Lys Lys Lys Ile Lys Trp Ile Gly Leu Thr Thr Asn
            180                 185                 190
Ser Ala Gln Asn Cys Gln Asn Leu Arg Val Glu Arg Gln Lys Arg Leu
        195                 200                 205
Glu Arg Ile Lys Gln Lys Gln Ser Glu Leu Gln Gln Leu Ile Leu Gln
    210                 215                 220
Gln Ile Ala Phe Lys Asn Leu Val Leu Arg Asn Gln Tyr Val Glu Glu
225                 230                 235                 240
Gln Val Ser Gln Arg Pro Leu Pro Asn Ser Val Ile His Val Pro Phe
                245                 250                 255
Ile Ile Ile Ser Ser Ser Lys Lys Thr Val Ile Asn Cys Ser Ile Ser
            260                 265                 270
Asp Asp Lys Ser Glu Tyr Leu Phe Lys Phe Asn Ser Ser Phe Glu Ile
        275                 280                 285
His Asp Asp Thr Glu Val Leu Met Trp Met Gly Met Thr Phe Gly Leu
    290                 295                 300
Glu Ser Gly Ser Cys Ser Ala Glu Asp Leu Lys Met Ala Arg Asn Leu
305                 310                 315                 320
Val Pro Lys Ala Leu Glu Pro Tyr Val Thr Glu Met Ala Gln Gly Thr
                325                 330                 335
Phe Gly Gly Val Phe Thr Thr Ala Gly Ser Arg Ser Asn Gly Thr Trp
            340                 345                 350
Leu Ser Ala Ser Asp Leu Thr Asn Ile Ala Ile Gly Met Leu Ala Thr
        355                 360                 365
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Ser Ser Gly Gly Ser Gln Tyr Ser Gly Ser Arg Val Glu Thr Pro Ala
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385 390 395 400
Asn Asp Glu Asp Asp
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<223> ARP6

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aatattagag ataatatcca atgttggcaa gaaagagtaa acaagtatgt tggtgggaat 180
ataaaatgat acagcctttt gagaagataa tttgctatga tctagaaaaa tatttagtat 240
gcatcccatt tgacccagaa attccacact gaagtccata ttctacagag atatgaaccc 300
acgtgtaatt atatgattgt atatatttac atataagtgc aaaatatttt gaggtagcat 360
tgtttggaat agcatgatac tggggctggg tccagaggct cacacctata atcccagcac 420
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<212> DNA
<213> Homo sapiens

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<222> (0)...(0)
<223> ARP10

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cctcctgagc ccagctcctc tcctcacttg ttgactaagc cctgcttcac tgagcatttt 180
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gccatcagtc agtagaacaa atgggcttgc tctgcctaac atcgggccat ctcggattcc 300
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acacatcagg ggccagctcc tagcactaaa tcacgctacg gcatacatct gttatcggac 420
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<223> ARP12

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<211> 521
<212> DNA
<213> Homo sapiens

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<223> ARP18

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ttttggagaa attgacttac cataccactc atcaacccat gcaaaagcct gtctatgtcc 180
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ctttgatgaa aactatctgg aagacaagtt gttaacaatt ctggggatct tggtgattac 300
agagttctta atcctctgt ccataggtga tgacaattac aggctgccta taggtcctat 360
agtgctcaca cacctccagc ccttccccat ggtgtacaca cacttgcagt atattcatct 420
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<210> 29
<211> 644
<212> DNA
<213> Homo sapiens

<220>
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<222> 591
<223> n = A,T,C or G

<221> misc_feature

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tctttcttat ttatatcatc tccaagtacc tctggctcct ttcctcttgc tcaccggarc 480
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gcttaggacc acccaccatg cctatccagg tgctgaaggg cctgaccatc actcattaag 180
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aaa atc ccc atg aat gaa ctg aca aca atc ctg aag gcc tgg gat ttt   879
Lys Ile Pro Met Asn Glu Leu Thr Thr Ile Leu Lys Ala Trp Asp Phe
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Leu Ser Glu Asn Gln Leu Gln Thr Val Asn Phe Arg Gln Arg Lys Glu
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tct gta gtt cag cac ttg atc cat ctg tgt gag gaa aag cgt gca agt   975
Ser Val Val Gln His Leu Ile His Leu Cys Glu Glu Lys Arg Ala Ser
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atc agt gat gct gcc ctg tta gac atc att tat atg caa ttt cat cag   1023
Ile Ser Asp Ala Ala Leu Leu Asp Ile Ile Tyr Met Gln Phe His Gln
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cac cag aaa gtt tgg gat gtt ttt cag atg agt aaa gga cca ggt gaa   1071
His Gln Lys Val Trp Asp Val Phe Gln Met Ser Lys Gly Pro Gly Glu
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gat gtt gac ctt ttt gat atg aaa caa ttt aaa aat tcg ttc aag aaa   1119
Asp Val Asp Leu Phe Asp Met Lys Gln Phe Lys Asn Ser Phe Lys Lys
 95                  100                 105                 110

att ctt cag aga gca tta aaa aat gtg aca gtc agc ttc aga gaa act   1167
Ile Leu Gln Arg Ala Leu Lys Asn Val Thr Val Ser Phe Arg Glu Thr
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Glu Glu Asn Ala Val Trp Ile Arg Ile Ala Trp Gly Thr Gln Tyr Thr
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Lys Pro Asn Gln Tyr Lys Pro Thr Tyr Val Val Tyr Tyr Ser Gln Thr
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Pro Tyr Ala Phe Thr Ser Ser Ser Met Leu Arg Arg Asn Thr Pro Leu
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ctg ggt cag gag ttg aca att gct agc aaa cac cat cag att gtg aaa   1359
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175                 180                 185                 190

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Met Asp Leu Arg Ser Arg Tyr Leu Asp Ser Leu Lys Ala Ile Val Phe
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aaa cag tat aat cag acc ttt gaa act cac aac tct acg aca cct cta   1455
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cag gaa aga agc ctt gga cta gat ata aat atg gat tca agg atc att   1503
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cat gaa aac ata gta gaa aaa gag aga gtc caa cga ata act caa gaa   1551
His Glu Asn Ile Val Glu Lys Glu Arg Val Gln Arg Ile Thr Gln Glu
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aca ttt gga gat tat cct caa cca caa cta gaa ttt gca caa tat aag   1599
Thr Phe Gly Asp Tyr Pro Gln Pro Gln Leu Glu Phe Ala Gln Tyr Lys
255                 260                 265                 270

ctt gaa acg aaa ttc aaa agt ggt tta aat ggg agc atc ttg gct gag   1647
Leu Glu Thr Lys Phe Lys Ser Gly Leu Asn Gly Ser Ile Leu Ala Glu
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agg aaa gaa ccc ctc cga tgc cta ata aag ttc tct agc cca cat ctt   1695
Arg Lys Glu Pro Leu Arg Cys Leu Ile Lys Phe Ser Ser Pro His Leu
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ctg gaa gca ttg aaa tcc tta gca cca gcg ggt att gca gat gct cca   1743
Leu Glu Ala Leu Lys Ser Leu Ala Pro Ala Gly Ile Ala Asp Ala Pro
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ctt tct cca ctg ctc act tgc ata ccc aac aag aga atg aat tat ttt   1791
Leu Ser Pro Leu Leu Thr Cys Ile Pro Asn Lys Arg Met Asn Tyr Phe
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Lys Ile Arg Asp Lys  *
335

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Lys	Val	Trp	Asp	Val	Phe	Gln	Met	Ser	Lys	Gly	Pro	Gly	Glu	Asp	Val
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Thr	Lys	Phe	Lys	Ser	Gly	Leu	Asn	Gly	Ser	Ile	Leu	Ala	Glu	Arg	Lys
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325 330 335
Arg Asp Lys